UNITED STATES OF AMERICA

DEPARTMENT OF HEALTH AND HUMAN SERVICES

FOOD AND DRUG ADMINISTRATION

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CENTER FOR DEVICES AND RADIOLOGICAL HEALTH

MEDICAL DEVICES ADVISORY COMMITTEE

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DEVICE GOOD MANUFACTURING PRACTICE ADVISORY COMMITTEE

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April 11, 2013
8:00 a.m.

Hilton Washington DC North
620 Perry Parkway
Gaithersburg, Maryland

PANEL MEMBERS:

RONALD J. ZABRANSKY, Ph.D.	Chair
BRENDA E. ARMSTRONG, M.D.	Health Profession Representative
MARY D. OLIVERA, M.S., CRCST	Health Profession Representative
ELIZABETH K. BLACKWOOD, M.S.	Industry Representative
CECILIA L. KIMBERLIN, Ph.D., RAC	Industry Representative
DAVID C. CRANMER, Ph.D.	Government Representative
EDNA FIORE, MT (ASCP)	Patient Representative
TERRY D. SCHUENEMEYER, RN	Public Representative
NATASHA G. FACEY	Designated Federal Officer

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JENNIFER KELLY, Ph.D.
Commissioner's Fellow
Office of Compliance

JAN WELCH
Deputy Director for Regulatory Affairs
Office of Compliance

CAPT KIMBERLY LEWANDOWSKI-WALKER
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Director of Special Projects
Assistant Secretary of Preparedness and Response (ASPR)
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Independent Emergency Manager

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Field Investigator, New England District Office
FDA

INDEX

INDEX

M E E T I N G

(8:00 a.m.)

DR. ZABRANSKY: I'd like to call this meeting of the Device Good Manufacturing Practices Committee of the Medical Device Advisory Committee to order.

I am Dr. Zabransky. I am the Chair for this particular meeting. I am a retired clinical and public health microbiologist. I was most recently at the VA in Cleveland, Ohio, and Professor of Pathology at Case Western Reserve Medical School. Currently I do some consulting work for clinical laboratories.

I'd like now to introduce -- have the Committee introduce themselves, giving their area of expertise, their affiliation, and their particular position on the Committee, whether they are an Industry Rep or Public Rep.

Thank you. We'll start over here with Ms. Olivera.

MS. OLIVERA: Good morning. My name is Mary Olivera. I am a health professional, and my affiliation is with OSPECS consulting. My expertise is in sterile processing in operating room.

MS. SCHUENEMEYER: Good morning. My name is Terry Schuenemeyer. I am a nurse by training, and I've worked in clinical research on the industry side and the academic side. I'm currently the regulatory affairs professional for the Methodist Hospital Research Institute in Houston, Texas.

MS. FIORE: I'm Edna Fiore. I'm a patient advocate, and I also have a background of 35 years as a clinical laboratory scientist.

MS. BLACKWOOD: Good morning. I'm Liz Blackwood. I'm representing industry today, 25 years in medical devices and pharmaceuticals. I'm a mechanical engineer by training and currently the Vice President of Quality Systems at Johnson & Johnson.

DR. KIMBERLIN: Good morning. My name is Cecilia Kimberlin. I am an Industry Representative on the panel. I have 27 years experience in the medical device industry and R&D, quality and regulatory affairs, and I have recently retired and am acting as an independent consultant for medical device companies.

DR. McNAMEE: Good morning. My name is Scott McNamee. I'm in the Office of Compliance at CDRH. I serve as the Special Assistant for Science to the Director of the office. I've been with the Agency almost 20 years, 10 years in the lab and 10 years in compliance. My background is material science engineering.

MS. WELCH: Good morning. My name is Jan Welch. I work for FDA in the Office of Compliance. I'm the Deputy Director for Regulatory Affairs. I guess I've been with FDA 23 years. I was a specialist in medical technology by training. Before I came to FDA, I worked at CBER. I've been at CDRH for about 20 years. And so I've been on both sides of the Quality System regulation, starting with the old GMP regulation. Learned that. And

so I've sort of shepherded and been quite involved with the Quality System regulation ever since.

Thank you.

DR. CRANMER: Good morning. I'm Dave Cranmer. I'm the Government Representative, and I'm with the National Institute of Standards and Technology. My Ph.D. is in material science and engineering, but in the past 23 years I've been in the NIST manufacturing extension program. We, in fact, help small manufacturers stay competitive in this country so they can compete globally, and we have had an active practice in continuity of operations planning.

DR. ARMSTRONG: Good morning. I'm Brenda Armstrong, a professor of pediatrics and pediatric cardiovascular medicine. I was chief of the pediatric cardiac catheterization laboratory at Duke University Medical Center for the past 18 years, and my training is in pediatric cardiology and cardiovascular medicine.

MS. FACEY: Natasha Facey, Designated Federal Officer for the Device Good Manufacturing Practice Advisory Committee at FDA.

DR. ZABRANSKY: Thank you all. And welcome. As you can see, we have a broad spectrum of expertise and every proper representation.

I note for the record that the voting members present here constitute a quorum as required by the 21 C.F.R. Part 14. I would also like to add that the Committee participating in the meeting today has received

training in FDA device law and regulations.

For today's agenda, the Committee will be discussing the potential effects of extreme weather and natural disasters on medical device manufacturing chain processes and marketed medical device safety and quality.

Before we begin, I would like to ask our distinguished Committee members -- oh. Okay, yeah.

If you have not already done so, please make sure that you sign the attendance roster out in the lobby.

And Ms. Natasha Facey, who was introduced before, the Designated Federal Officer for the Device Good Manufacturing Practice Advisory Committee, will now make some introductory remarks.

Natasha.

MS. FACEY: The Food and Drug Administration is convening today's meeting of the Device Good Manufacturing Practice Advisory Committee under the authority of the Federal Advisory Committee Act of 1972. With the exception of the Industry Representatives, all members of the Committee are special Government employees or employees of any State government or of the Federal government and are subject to Federal conflict of interest laws and regulations.

The following information on the status of this Committee's compliance with Federal ethics and conflict of interest laws covered by, but

not limited to, those found at 18 U.S.C. Section 208 are being provided to participants in today's meeting and to the public.

FDA has determined that members of this Committee are in compliance with Federal ethics and conflict of interest laws. Under 18 U.S.C. Section 208, Congress has authorized FDA to grant waivers to special Government employees and regular Government employees who have potential financial conflicts and when it is determined that the Agency's need for a particular individual's services outweighs his or her potential financial conflict of interest.

Related to the discussions of today's meeting, members of this Committee who are special Government employees and employees of State government and of Federal government have been screened for potential financial conflicts of interest of their own as well as those imputed to them, including those of their spouses or minor children and, for purposes of 18 U.S.C. Section 208, their employers. These interests may include investments; consulting; expert witness testimony; contracts/grants/CRADAs; teaching/speaking/writing; patents and royalties; and primary employment.

For today's agenda, the Committee will discuss the potential effects of extreme weather and natural disasters on medical device manufacturing chain processes and marketed medical device safety and quality. Extreme weather events and natural disasters can interfere with the manufacturing, shipping, storage, or use of marketed devices, which may lead

to concerns with their safety or effectiveness. Examples of such events include hurricanes, floods, lightning storms, earthquakes, and fires. The Committee will further discuss how to optimize the use of FDA's current regulatory framework and to address risks and vulnerabilities to the manufacturing chain resulting from extreme weather conditions. Further steps may be identified to help industry mitigate or better tolerate challenges to the manufacturing chain as a result of extreme weather conditions. FDA is requesting comments on the following three scenarios related to medical devices and extreme weather: Scenario A, Marketed devices already in use for patient care; Scenario B, New and/or used devices, components or accessories; and in Scenario C, Damage to medical device manufacturing sites.

Based on the agenda for today's meeting and all financial interests reported by the Committee members, no conflict of interest waivers have been issued in accordance to 18 U.S.C. Section 208. A copy of this statement will be available for review at the registration table during this meeting and will be included as a part of the official transcript.

Ms. Elizabeth Blackwood and Dr. Cecilia Kimberlin are serving as the Industry Representatives, acting on behalf of all related industry. Ms. Blackwood is employed by Johnson & Johnson, and Dr. Kimberlin is employed by Kimberlin, LLC.

We would like to remind members that if discussions involve

any other products or firms not already on the agenda for which an FDA participant has a personal or imputed financial interest, the participants need to exclude themselves from such involvement and their exclusion will be noted for the record. FDA encourages all other participants to advise the Committee of any financial relationships they may have with any firms at issue.

For the duration of the Device Good Manufacturing Practice Advisory Committee meeting on April 11th, 2013, Ms. Edna Fiore has been appointed as a temporary voting [sic] member.

For the record, Ms. Fiore serves as a consultant to the Pulmonary Allergy Drugs Advisory Committee at the Center for Drug Evaluation and Research. This individual is a special Government employee who has undergone the customary conflict of interest review and has reviewed the material to be considered at this meeting.

The appointment was authorized by Jill Hartzler Warner, J.D., Acting Associate Commissioner for Special Medical Programs, on April 2nd, 2013.

Before I turn the meeting back over to Dr. Zabransky, I would like to make a few general announcements.

Transcripts of today's meeting will be available from Free State Court Reporting, contact number (410) 974-0947.

Information on purchasing videos of today's meeting can be

found at the table outside the meeting room.

The press contact for today's meeting is Synim Rivers.

I would like to remind everyone that members of the public and press are not permitted in the Committee area, which is the area beyond the speaker's podium. I request that reporters please wait to speak to FDA officials until after the Committee meeting has concluded.

If you are presenting in the Open Public Hearing session today and have not previously provided an electronic copy of your slide presentation to FDA, please arrange to do so with AnnMarie Williams at the registration desk.

In order to help the transcriptionist identify who is speaking, please be sure to identify yourself each and every time you speak.

Finally, please silence your cell phones and other electronic devices at this time.

Dr. Zabransky.

DR. ZABRANSKY: Thank you.

At this time I'd like to welcome Mr. Steve Silverman, Director of the Office of Compliance in the Center for Devices and Radiological Health at the FDA, for some opening remarks.

MR. SILVERMAN: Good morning. It's nice to see you all. My name is Steve Silverman, and I'm the Director of the Office of Compliance in FDA's Center for Devices and Radiological Health. We all have important

work today, so I'm going to keep my comments mercifully brief.

I want to welcome the members of the Device Good Manufacturing Practice Advisory Committee. To say the least, it has been a number of years since this Committee has met, and we're very happy to now bring to the Committee a matter for discussion that is both of the moment and significant.

Our office's mission is to protect the public health by evaluating, enhancing, and ensuring compliance with medical device laws, resulting in the availability of high-quality medical devices, and we work to achieve that goal through multiple mechanisms. These include some mechanisms that are responsive to identifying violations and some of which are forward looking in order to prevent violations.

But no matter what the mechanism is that we apply, to be effective we must understand the environment in which we operate, and this includes, as will be discussed today, understanding the impact of extreme weather events on medical device production and distribution. We define these events as unusual, severe, or unseasonable weather, or weather at the extremes of the historical distribution that is in the range that has been seen in the past.

And we don't need to look very far to find examples of extreme weather. Whether we look to Hurricane Sandy, the 2011 tsunami that devastated Japan, or the damage threatened by heavy rains and wildfires in

the West, it's clear that catastrophic events in nature can jeopardize a device maker's capacity to make and market safe and effective medical devices. As significant, these events threaten the well-being of the patients who use these devices, some of whom rely on them to prevent or treat life-threatening conditions.

So in considering these challenges and understanding the threats posed by extreme weather, and in identifying how the FDA can work with device makers and users to prevent and mitigate risks, we are here today to ask for your help. Today we'll seek your input on a number of key questions.

How can the FDA apply its regulations to help assure that both during and after extreme weather events, the integrity of devices during transport, storage, and use is maintained?

What actions should device makers take to quickly return to full production after an extreme weather event?

What elements of the device Quality System regulation are critical for manufacturers to control production, transport, and storage in the aftermath of an extreme weather event?

What kinds of controls should device makers apply to component suppliers that are affected by extreme weather, to minimize risks to safety and device performance?

And in the positive column, does the prospect of extreme

weather events create opportunities for increasing the robustness of medical devices to withstand extreme and austere environments?

The input that you each will provide today will help us to grapple with these critical questions, and we will use that information to help us address known and serious threats to public health.

Again, I want to thank you for your time and your commitment to the welfare of medical device users, and I want to turn the process back to our Committee Chair, Dr. Zabransky.

Thank you.

DR. ZABRANSKY: Thank you very much, Dr. Silverman.

We will now proceed to the FDA's first presentation.

I'd like to remind public observers at this meeting that while this meeting is open for public observation, public attendees may not participate except at the specific request to me.

The Committee will now hear from Dr. Jennifer Kelly on the extreme weather project.

Dr. Kelly, welcome.

DR. KELLY: Thank you. And welcome. My name is Jennifer Kelly, and I've been working on this topic in the Office of Compliance in CDRH, and I'm really excited to have everyone here today and look forward to today's discussion. So without further delay, let's get to today's program.

So you will be hearing from three FDA presentations this

morning. First, I will give a presentation and address the extreme weather project and how extreme weather events may threaten many areas of the medical device industry.

Second, our Deputy Director of Regulatory Affairs, Ms. Jan Welch, will speak on to specific parts of the current regulatory framework and how they meet challenges to the industry from extreme weather events.

And, third, we'll have Captain Kimberly Lewandowski-Walker, a national expert of medical devices, give an ORA compliance program perspective and how medical device inspectors meet challenges of extreme weather events to the industry.

We'll have an open period for the general public, followed by a break for lunch, and then an open period for industry. FDA will address their questions to the Advisory Committee for you to discuss and offer recommendations for the FDA and industry.

So like I said, I'd like to talk this morning about how extreme weather events can threaten many areas of the medical device manufacturing chain, which could lead to concerns over medical device safety and quality.

Briefly, this morning I'd like to discuss a brief background of the extreme weather project and highlight specific conditions and examples of extreme weather and how they may intersect to make challenges to medical device safety and quality. I hope I can illustrate how we can break this down

and identify three main focused areas, so devices used in extreme weather events or in the aftermath of a natural disaster, devices and components caught in extreme weather, or manufacturing processes caught in extreme weather events. And I'll finish up with a summary.

So the extreme weather project really started with internal discussions in the wake of Hurricane Katrina, when a fungal contamination in contact lens solutions resulted in a severe public health risk. A Commissioner's Fellowship was funded in 2011, and this project started in November to really take a deeper look at these events and how they may make medical device safety and proper function vulnerable.

This is a snapshot of billion-dollar weather disasters from 1980 to November of 2011. We're talking about earthquakes, hurricanes, windstorms, wildfires, dust storms, hailstorms, blizzards, extreme flooding, and many more.

And we know that these natural disasters and extreme weather events aren't unique to the United States. It's really a global phenomenon. So this global map highlights in circles economic losses related to storms and hail, flooding events, extreme weather, earthquakes, tsunamis, and volcanoes

And so just like natural disasters are really a global phenomenon, so is the medical device industry. So you can have a component supplier in New Zealand inundated with an earthquake, results in a tsunami, and they can't ship. They have to halt all shipments to deliver

their component to a medical device maker in Brazil. They can't complete their production, so their shipment of critical life-sustaining equipment to a hospital in Minnesota is delayed or canceled.

So what kind of threats of these events may really result to impact and affect medical device safety and use, which ultimately will affect the public health? So power outages, network outages, severe flooding, extreme temperature levels, extreme levels in humidity, dust storms, fires, contamination of your water supply, and transport interruptions may all have an effect on the medical device industry.

And to put things into better perspective, I'd like to highlight a few specific examples and the conditions of these extreme events and how they intersect with the medical device industry.

So Hurricane Katrina in 2005 became the costliest national disaster and one of five deadliest hurricanes in U.S. history. It affected 90,000 square miles.

This is an image, on the left, of much of New Orleans under water, completely flooded. This storm interrupted dialysis services throughout the Gulf Coast and left millions of people without electricity for several weeks. This storm, like many of such severity, really highlight the importance of being able to access fresh water.

To put things into context, a healthy patient may require 14 liters of water per week, while patients requiring dialysis treatment may need

between 350 to 500 liters per week. And other medical devices that require water for proper function include IV pumps. And your system may become overstressed or even more challenged when you have pathogens contaminating your water system. So is your water filtration system even capable of decontaminating such pathogens? Do you even know the pathogens exist?

With extensive power outages like the one that followed Hurricane Katrina, critical devices requiring electricity in hospitals and homes may also be affected. So ventilators, insulin pumps, glucose meters, apnea monitors, and others may not be able to last on backup battery power supply very long, or increased challenge when you find that your backup battery supply is out of date, or your backup power generator becomes flooded or is supplying dirty electricity.

Often, when regular power is restored, devices reset to default settings. That may affect the care of a patient, if the patient or the caregiver doesn't recognize that the settings may have changed.

And also with extensive power outages, one often loses Environmental Controls. So you're not going to have an air conditioning or a fan running in the summer heat of New Orleans. So some components or materials packaging of medical devices may not be meant to withstand such extreme levels of heat and humidity.

Another example I'd like to touch on occurred in 2011. Japan

suffered a 9.0 magnitude earthquake, which resulted in a tsunami with waves as high as 40.5 meters, or 133 feet. This resulted in really a nuclear emergency. Their nuclear power plant became damaged and flooded, and a part of the widespread damage was structural damage, fires, a dam collapsed, and a lot of contamination.

These events resulted FDA to put all regulated products on import alerts. For devices, concern was over possible radioactive contamination of raw materials inside the fallout zone. Concerns were over possible water-damaged electrical components, compromised sterility, and product shortages. This really prompted the need for additional and unusual testing of materials that may have been affected by the tsunami.

A super storm, called a super derecho, happened in June of 2012, last year. This is a radar shot of the unique bands of the severe storm covering about 450 miles in six hours, in this shot, through the Midwest and Ohio Valley. It contained hurricane-force winds and violent thunderstorms and spanned much of the country, a total trail of destruction covering 700 miles in 12 hours.

This severe storm, again, left widespread damage from downed trees and electricity poles and lengthy power outages. Cell service was down. 911 calling, servicing 3.6 million people, was partially or completely out for several days. And this was in a heat wave in D.C. and Midwest, so medical devices may have been affected again without regular power, network

connections, and loss of environmental controls.

Another super storm, or Hurricane Sandy, as mentioned earlier, hit the East Coast in October of last year. This map from FEMA shows the widespread nature of the impact of the storm. Fourteen states were affected. Millions were without power for days to weeks; 305,000 homes were destroyed in New York State alone.

This is a view of the New York skyline of lower Manhattan, and with the exception of one building, it's in complete darkness due to a preventative power outage caused by Sandy. So 2.2 million were without power; 265,300 businesses were affected. And, again, communication infrastructure was out, including wireless services and fiberoptic cable services.

Four hospitals in the New York area had to evacuate during Sandy. New York University Langone Medical Center, Coney Island Hospital, the Manhattan VA, and Bellevue Hospital all had to evacuate their patients during the storm. And this was largely due to flooded backup emergency power generators. Patients ranged from cardiac patients to preemies, and patients really had to, in some cases, be transported down dark stairwells with medical devices still attached for continuous treatment and monitoring. Clinical trials were even affected in this area.

The flood levels reached the street levels of New York. This is an image of the Brooklyn-Battery Tunnel under water. And so the flood levels

were really unprecedented and unexpected, and as a result, major transportation arteries are interrupted and cannot be used. Flooding also inundated facilities and warehouses. 266 facilities of FDA-regulated products had flooding and damage. Of those, 54 facilities were from medical device firms. So you can imagine, device packaging and components may not be able to withstand such environments when it comes into your warehouse.

This is a North Carolina highway damaged from Hurricane Sandy. So what types of effects did Hurricane Sandy have on transportation? 20,254 flights were canceled, train services were down up and down the ;eastern corridor, and damaged roads are estimated to cost a little less than $1 billion in New York State alone to repair.

What does that mean for the medical device industry? You may have had delays in restocking supplies for hospitals, for clinics, for home-use equipment; delays in shipping of medical devices, components, raw materials. The just-in-time manufacturing may be severely affected by such a storm. And, again, environmental controls may be lost when there are interruptions and delays and you can't move product forward.

With extreme conditions we include extreme drought. This is the U.S. Drought Monitor as of July 17, 2012, last year, and one can see that the Mississippi River system covers a good bit of the country. So this drought has been the worst draught in seven decades, and with one-inch water loss in the river system, barges have to unload 17 tons of cargo. With that, capacity

decreases with one-foot loss in the lower river section by 9,000 tons. This is a potential to halt a $180 billion transportation industry.

So the medical device industry may not heavily rely on barge transport. But when the grain export industry, when the petroleum industry, when the coal industry need to seek alternatives for pushing their product forward, it's possible that the medical device industry will feel that with increased costs and overstressed transportation networks.

This dust storm occurred in Phoenix in 2011. Desert thunderstorms kicked up a mile-high wall of dust and particles, reducing visibility to zero. And this was the worst dust storm since the Dust Bowl of the 1930s. Eight thousand customers were without power, and obviously the air quality was affected. So your asthma community, your devices that allow people to breathe better may have been affected. But also if you have medical device manufacturing processes that are conducted in dust-free rooms or clean-room settings, if their air-handling systems are overstressed, you may have particle or dust contamination on your device.

So this is the mapping of the firms in the Phoenix area, a little less than 1500 that may have been affected by this dust storm.

So one last natural disaster that I'd like to discuss was the Icelandic volcano eruption. The resulting ash cloud really impacted much of the European air space. So their air space had to be closed due to this ash cloud, the highest level of air travel disruption since World War II. Twenty

countries and 100,000 travelers were affected. And so you can imagine that general shipment delays and pushing medical products forward may have been interrupted due to this air space closure.

But the nuclear medicine was especially affected. So 80% of nuclear medicine and medical scans rely on one type of radioisotope, technetium, and due to its short half-life of six hours, it's impossible to stockpile. So when there were orders that couldn't be completed during this time, doctors had to rely on costlier and older alternatives or not just have as many scans.

So we recognize that natural disasters can also have similar effects as manmade disasters. So, for example, a plant explosion, like the Evonik's plant explosion last year, can have similar ripple effects to the medical device industry. This plant produced over 75% of the world's precursor material to nylon 12. Nylon 12 is a material used in the medical device industry, but also in the auto industry, which made this an extremely more challenging situation. Nylon 12 is used in cardiac devices, stent delivery systems, ventilators, and many more. And so FDA really had to bring together desperate stakeholders to avoid shortages of materials and devices.

So I hope I have been able to illustrate how we can break down this vast area of concern to three focuses, medical devices used in extreme weather or in the aftermath of a natural disaster.

So medical devices requiring electricity and network

connections may become especially vulnerable; devices requiring filtered water; life-sustaining equipment that is really crucial to properly function in the aftermath of a disaster. And then devices and components especially sensitive to austere environments and extreme environments may just not be meant to be used under those conditions.

Second, medical devices and components caught in extreme weather, so raw materials that may be contaminated in a fallout zone or near contaminated flooded waters. Transportation interruptions may disrupt the environmental controls, or overstressed packaging may lead to failure or adulterated products.

Third, manufacturing processes caught in extreme weather, so damage from flooding to a facility or a warehouse, power outages during ongoing manufacturing processes, water needed in washing steps may become contaminated without you knowing and you may not have a filtration system to account for that.

So, in summary, I hope I have illustrated how extreme weather and their conditions can affect medical devices and the industry in many ways. Device production, shipping, storage, and proper function may become vulnerable under these extreme weather events. And device design may not have the robustness built into it to withstand such extreme weather events and conditions.

So how can successful practices of the regulatory framework

reduce the risks from extreme weather? Redefining a rare event may lead us to redefining what successful practices are.

With that, I'll leave you with one last image.

Thank you for your attention, and I'd be happy to take any questions.

DR. ZABRANSKY: Thank you very much, Dr. Kelly.

Does anybody on the Committee have any questions for Dr. Kelly that she can expand upon or clarify? If not and if you think of any later on, we can come back to this and address this later on during our deliberations.

DR. CRANMER: I have one.

DR. ZABRANSKY: Go ahead.

DR. CRANMER: This is Dave Cranmer.

In listening to your discussion of all of the potential vulnerabilities in the supply chain, it strikes me that there are both manufacturing supply issues as well as location issues that have risks associated with them.

For the manufacturing processes themselves, have you given any thought to applying lean manufacturing techniques, like value stream mapping, to look at an entire supply chain of an OEM to try and identify and maybe start to quantify what some of those risks might be?

DR. KELLY: That's an excellent point. I think, as far as our

mapping capability and data that we have, we've been trying to see if there are certain hot spots or some processes that – can go smoothly. I'm not sure how much data we have available to really address that. I'm not sure if my colleagues may have better answers.

DR. McNAMEE: This is Scott McNamee.

No, I don't think we have that capability, but if we can connect off line, it would be very interesting to see if that's something that we might be able to apply in the future.

DR. CRANMER: This is one of those agency-to-agency things I think we can work out, but it clearly requires that the companies themselves be willing participants.

DR. KIMBERLIN: I would comment that many companies do integrate such practices into both their design phase as well as post-design and design transfer into manufacturing. I'm not sure it's consistent across the entire industry, but we could all benefit from sharing lessons learned. And it's one thing to read and train about those best practices, but to actually implement them in such severe situations is really important, and to do it in advance of these types of potential outcomes. So I really appreciate your comment, too.

DR. ZABRANSKY: Dr. Kelly, I'd like to add some other manmade disasters to your list. A number of years ago there was a nuclear accident in Russia that created a real problem for them. And then we had in Harrisburg,

Pennsylvania, a number of years ago in the United States, we had a nuclear accident. And again going back to Russia, they had an anthrax problem which affected a large area. Now, that was also manmade. We don't know what that did to the communities around that area.

DR. ARMSTRONG: I have a question. It seems to me that part of the oversight or part of the planning, especially where resources that affect or intersect human health are concerned, that there would be some oversight with respect to planning within new hospital structures or new health facility structures that would mitigate looking at just the variables that you have so nicely demonstrated this morning.

Is there any thought given to attaching an oversight function as new hospitals come on line, or as hospitals that are already on line begin to look at the aftermath of disasters, model those and reorganize their resources to address those potential disasters, since it seems that they're coming in greater frequency and in greater magnitude?

DR. KELLY: That's a great point. We've been working with colleagues that have a network of MedSun hospitals, and we can reach out to them and talk to their clinical engineer and have questions and have them answer a survey. I think, as I understand it, it's a volunteer basis and that the FDA doesn't regulate hospitals or the medical care in hospitals. But I think if people are open to working together and seeing what is a successful practice versus what's happened to the flooding in hospitals in New Orleans and New

York, the tornadoes in Joplin, if there are some successful practices and hospitals want to work with us, I think that we'd be open to it. But as I understand it, FDA has no oversight of where they put what supplies and how much.

DR. ARMSTRONG: It would seem to me that those discussions really need to occur in earnest.

DR. ZABRANSKY: Thank you very much again, Dr. Kelly.

I'd like to remind the Committee members to please state your name before you ask your question or make a comment. This would help the recorders over here figure out who's talking.

We will now proceed to the next presentation by the FDA.

I'd like to remind any public observers at this meeting that while this meeting is open to the public, you cannot participate except at request to me.

The Committee will now hear from Ms. Jan Welch on the Quality System regulation.

Ms. Welch, please.

MS. WELCH: Thank you. Good morning.

I wanted to sort of do a little historical note here for a second. So this is my copy of the preamble in the regulation that I've been carrying around since October 7th, 1996, so pretty well used, my copy of the reg. And I did a little reading. I knew when the last Advisory Committee was. I didn't

attend, but it was September 13th and 14th, 1995, so that's 18 years ago or just about 18 years ago. So we can all sort of pause and think where we were in particular, you know, in September of 1995. And it's an interesting reason why the Committee met at that time, and I think it's a good segue into the little presentation that I'm going to give you about the regulation and its nexus to these events.

The Committee met then because it was the last working draft to the regulation. And so you put this in context of why did we have the Quality System regulation then in 1995 and 1996? What was insufficient or what was inadequate about the 1978 GMP regulation, which had served the Agency and the medical device community for 18 years?

So I wouldn't say that the '78 reg was proscriptive, but it wasn't robust when we got into the '90s and it really lacked design control provisions. So I'm going to talk about that a little bit because that was one of the key provisions that went into the new regulation -- we call it new -- then in 1996. And it's still today. When I make some comments about the reg and these connections, it is probably one of the most critical points in the system, in terms of assessing device quality and device safety, and it's used in these different situations.

So when we enacted this new reg with the input from the device GMP advisory panel on this working draft back in 1995, our reg was intended to be flexible. It was intended not to be proscriptive. And so it was

intended to meet the needs of every medical device manufacturer, whether they were the two-person or five-person company, of which we regulate several, as well as the tens-of-thousands-of-employee companies that are global. So this one regulation had to span across all of these, as it does today, and I still think that that's the beauty of our regulation, of this reg.

And so I kind of wanted to put that in historical context. And here we are 17 years later, so we're getting into a cycle with these regs, right, and the advisory panels. Here we are 17 years later convening this panel. But, again, I think it's going to go to this examination of how the reg is implemented, what are the parts systemically in the reg that address these different points.

So what I'm going to do, when I asked Jennifer how long I had, she said I have 30 minutes. Thirty minutes is not a lot to talk about the Quality System regulation. You can spend hours and days on this. So what I want to do is highlight some of the key parts of the reg that, I think, have this impact for when manufacturers are designing their product, when they're redesigning their product, when they're thinking about its use in normal operating conditions, and when they're thinking about those extremes, because that's really sort of the issue at point today.

Risk analysis, I think, is key. I'm going to talk about that a little bit in design validation because that's really the heart and soul of where the consideration of impact is. And if it's not done right and well up front in this

design control subsystem, it has serious ramifications. And we see this on day-to-day normal activities, and I think that's exacerbated in extreme conditions.

All right. This is clearly not every part of the Quality System reg, and I'm not even going to talk about all of these. But some of these parts of the reg, as you listened to Jennifer and she was talking about supplies of components and she was talking about environmental controls, well, this sort of maps to -- these are the parts of the reg that really fit in with those elements and those experiences. And I'm just going to really focus in on some of the key ones and just sort of tease up to some of the questions that we will be asking of you this afternoon, so kind of to put some context.

So from the very beginning, when manufacturers are thinking about their product and they're thinking about how it's going to be used, where it's going to be used, who's going to be using it, are these professionals? Is this a home-care product? All of that goes into this at the very beginning in this design input, when these requirements are being collected and they're thinking about this intended use.

We need to think about normal environmental conditions, normal operating conditions. But then, truly, what are all the ways that we can envision, at that time, how a product will be misused? And I tell you, in a lot of years of experience, and I'm sure my industry colleagues know as well, even if you think that you've explored the gamut of how a product can be

misused, if you think of all of the ways that you could possibly put the wrong condition, the wrong place at the wrong time, we can't think of it all. You know, we can't think of it all.

And it's not FDA's expectation that manufacturers get this right and that it's frozen in time at the point that all of these process risk analyses and product risk analyses are being done. It's not possible. But it's the best at that time that that product comes in to FDA to be cleared or approved and then what's gained in the experience afterwards, all right?

So design validation really is sort of one of the hearts and souls of that part of the design control requirements that we put into the regulation in 1996, so a very, very powerful part of the regulation because this is where FDA's one explicit requirement for risk analysis resides in the regulation. So we talk about that, clearly, the manufacturers are looking at what is a normal operating condition.

But it's during this time when they're doing design validation and design reviews that the firms have to get all of their best minds together, their departments together, and think what are all of the potential fault conditions. You know, what are all of the things that could potentially go wrong? And this goes from human factors, this goes to material science, this goes to production and process, this goes to environmental impact. It's all of these things come together in order to do these risk analyses. And these are put through design reviews.

And I think that the most successful companies and very successful manufacturers have a robust design review and take this very seriously and have multiple people from multiple departments in there really trying to pick that apart and examine it, and others that just sort of do the perfunctory yes, I'm going to do one design review and be done and I've met the regulatory requirement. They're missing the point, they're missing the opportunity. This is just really a valuable place where this information is considered.

So, again, coming down to sort of the last couple of bullets and the one I put in red there, will -- you know, you have operating specs. So you've done validations, whether they're design validations or process validations, and so you have normal operating specs. And then again, in this process it's like okay, this is where I want things to be. But if they're outside of that a little bit, will it still be okay?

And part of that, as you'll see in some of these slides, are the considerations when we get into these disaster situations, when we get into these unforeseen circumstances. Okay, we have normal, we have operating, we've met specs. But if we go a little beyond that, is it still okay? Is it safe, is it effective, and in this situation, how far outside of that may we go, that's permitted to go, all right?

And so I would say that why I put this last bullet in red is to think about something for the Committee today, is that when manufacturers

are performing these risk analyses, is it something current? Are these extreme events, these really extreme events, you know, something that's being considered? Or is this something that the manufacturers need to be putting more proactively and prospectively into their system?

So purchasing controls and acceptance activities, two parts of the regulation that really fit hand in hand together. And clearly these days so much more is outsourced than it was in 1996. It was really amazing, when we promulgated this reg back then, so much manufacturing was done in house. So this whole notion of component suppliers and the like, it wasn't quite as critical as it is today. We have virtual manufacturers. FDA will go in and do some inspections, and we really are doing a paper and electronic audit because so much is outsourced.

So we were really forward thinking when we put this one part into the Quality System reg on purchasing controls, 820.50(a) and (b). Simple. Two paragraphs in the regulation, and it's amazing how effective and how critical those two parts of the regulation are. And it's a balance that they have together with acceptance activities that manufacturers are doing on a daily basis for all of their goods and services.

So in a normal operating scenario there's this balance. They know how much auditing they're going to do, how much sampling they're going to do, how much testing they're going to do. However, when you introduce a non-normal circumstance, a rare event, a disastrous event, then

what is going to happen with that balance? What is going to need to be prepared and ready in that Quality System to deploy to change that balance that's being used? This is especially critical when it comes to a sole supplier.

I mean, manufacturers struggle with this every day, and they take a risk when they do this. With critical components or critical supplies, if it's a sole supplier, that's a very risky business. And sometimes we know that there are component manufacturers, that that is the only ingredient, the only item that the manufacturer will need or will use, so it's putting a lot of eggs in that one basket.

And so then, when you put another one of these scenarios in here -- and Jennifer talked to you about nylon 12. That turned out not to be a major impactful situation, but boy, it sure could have. If that plant hadn't been able to get back up and running and hadn't been able to continue, there would've been manufacturers that seriously would've been impacted, and therefore the patients in the United States would've been impacted as a result of that.

So when we get into one of these disaster or non-normal operating situations, I think the manufacturers really have to then adjust their balance and their rubric, if you will, of incoming testing. They will have to do more, and they'll have to be prepared to do that. And manufacturers already have that now, because they watch and monitor their suppliers, and when they start to see problems, when their supplier audits aren't quite up to

snuff or they're seeing product that's coming in out of spec, they will adjust and they will increase sampling. They will do whatever they need to, but this takes it to a whole new level. So just again, it's not something that's being thought of perhaps on a daily basis, but what is it that the manufacturer may need in their Quality System that gets it prepared for that next level?

The regulation has provisions for once processes are validated, that there have to be controls in place. It's always about making sure that the process is repeatable, reliable, that it conforms, and that the device that's produced meets its specs. And so the reg has provisions for monitoring, for having those parameters assessed on a continual basis.

And so, again, now what will happen when there are interruptions, when there's going to be a specific event? What additional controls may need to be in place because those normal day-to-day controls may not? So, again, something that needs to be considered in these extreme events.

The regulation goes on, and we have some specific provisions for environmental controls and for contamination controls, and these obviously will come into play. You know, it's not just always on these extreme events too, but I'm sure manufacturers could say all right, I've had a plant where the roof just caved in one day. These things happen, right? Or maintenance has been going on and it's caused the roof on my aseptic filling room to leak or what have you. So these things happen on a daily basis,

regardless of a natural disaster.

So manufacturers have to then decide, okay, I had this material that was there in production, it was in this room, we had this. What am I going to do with it? So they already have to have these procedures there for quarantine of that material, assessing that material, you know, making the repairs. So these things happen, and I think that a good Quality System will have these mechanisms already in place. But then again, it's perhaps taking it to this next level where there's going to be production down for a much longer period of time, or I don't have an ancillary facility to turn to and get up to speed.

Process validation. So in the very beginning, as we were talking about it, I was talking about design controls. So processes are designed at the same time, all right, during this phase, and the processes have to work and they have critical parameters. So as basic process validation goes through, there are different phases. And in this operations qualification, or the OQ, phase of process validation, it's the expectation here that you're really trying to see where will my process fail. You're trying to take it and make sure you know where those parameters are. So where is my normal, well-defined operating band? But then where will I know that it fails? And so this is where manufacturers conduct design of experiments. They're trying to know their boundaries.

And then they get down to the next phase of process

validation, PQ, performance qualification, and they're getting to that normal. This is where I want to run. This is where I can control it. This is where I can see my variance. This is where I want to be.

But when we have one of these extreme events, then maybe, I think, it might be helpful for manufacturers to go back and look and have that data from OQ, from this operational qualification, there to say, well, okay, this is where I want to run, but I'm going back to some of that data, and if I go around some of that boundary, am I still okay? Am I still okay there?

And so these are some scenarios that I think, in these extreme situations, can go back to this data to see. Again, not ever sacrificing safety and efficacy, but as I said, there may be specifications a little bit outside that are still okay. So something to consider.

So nonconforming product. We have this part of the regulation, 820.90. Not all nonconforming product is created equal, if you will. And so manufacturers segregate and quarantine and have procedures for nonconforming product, and it's for a variety. It's a scale for what the nonconformity is. Sometimes it may be a very particular aesthetic or a cosmetic nonconformity, which has nothing to do with safety and efficacy, all the way ranging up to I've got a serious problem. I've got a spec for this component and I've got a spec for this supply, and I'm having major problems, and it needs to be segregated and not used. So the material review boards, or the processes that manufacturers use, vary to control

nonconforming product. And so this is again done on a daily, routine production basis.

But then what will be the scenario, what will be the next level for these processes in an extreme event? Again, looking for always perfect, tight, beautiful specs, but okay, now I can go back to I've got this emergency situation with that nonconforming product. I segregated it according to my procedures because I said it was nonconforming. But really is it acceptable? Can it be reconditioned? Is there some disposition that I can do with that? So this is a very key part of the regulation to control this product before it gets to production and before it gets out the door.

So the Corrective and Preventive Action piece, subsystem, if you will, of the Quality System is obviously very important when any situation, problem, nonconformity, arises. And so how the CAPA system is used in light of these extreme events is important. It may be, again, I want to emphasize, it's never about letting something out that's ineffective, that's unsafe, you know, not designed to do that.

But maybe, in these dire circumstances where patients are affected and they need to have the steady supply of product, and maybe this is a manufacturer of a sole product, that's when it gets to be very critical. Then, when you kind of drill down and use the CAPA system, it's perhaps using it more efficiently. Perhaps it's looking for short-term items that can be used for effectiveness checks, rather than I may not have the luxury of 90

days to look at the course of a correction or a corrective action, but I can't sacrifice, as I said, the safety meeting the specs. So it's got to be something really ramped up and controlled for 30 days to make sure that it's done well and corrected, but expedient. It's a balance in all of this.

Three other parts of the regulation certainly play in here. And I want to emphasize that these are all linked back to design inputs, design requirements. So the whole time the manufacturer is starting up with their design, these seem like sort of end-game issues, if you will, but they really have to be considered up front.

So packaging, handling, storage. The whole time all of these design inputs are being gathered it's like okay, am I shipping straight from my facility? Am I shipping to my distributors? Where are those going to be? Where are their warehouses? You know, am I in Alabama in the summer or am I in Minnesota in the winter? Where are these places that I am going to have my product distributed from? Talking about handling, storage, segregation, all of those need to be taken into consideration during the design.

So this afternoon, when we put these questions to you, think about this. Do you think that this is being done with forethought, if you will, for these extreme events? That's the connection.

And then we have a provision in the regulation, very much up in the front, 820.1(e), device exemption. And it's never really been used for

something of this nature. We had it in the old regulation, in the old '78 GMPs and we have it now, and really the only requesters that we've had, it's more been about a classification of the device or a general applicability. FDA often loves that people write in all the time, we don't think the regulation applies to us and our device. And we're like, well, yes, it does. Thank you and have a good day. So we cleared out a lot of these that way.

But I think about this provision in the regulation now because I think about the last 15 years, and not only about these extreme events, but I think back to 9/11 and I think about bioterrorism, we think about these things. So, again, we have this provision for a variance, for an exemption. So if there were this extreme, critical, dire situation, I put up here, consideration, this manufacturer might be the sole supplier of that device. Is there a benefit to could we relax some of the requirements of the regulation? And what would they be? So I wanted to sort of plant that seed out there too, because I think this is a silent option or a sleeping option that's out there.

All right. So just again trying to highlight what we see, I guess, the benefit of our FDA experience, what we see now just on a regular routine, monthly, weekly basis, where we see manufacturers use their Quality System to address daily problems, weekly problems, and where I think the parts of the regulation are key for when you take it to this next level for whatever this extreme might be, where will that come down to?

And I just think that in terms of risk analysis, I can't say enough about that, that I think that manufacturers that design well, that plan for risk analysis -- and one thing. I think that the most successful manufacturers constantly go back and reevaluate their risk analyses. They don't leave them there once, when they're designing their product, they submit their application and then they're done. I think the most successful manufacturers are going back, looking at their information all the time and going back and making reassessments on risk analysis. And that may be something that we have as an outcome here today, in terms of some guidance for manufacturing.

So with that, I think I'm concluded.

DR. ZABRANSKY: Thank you, Ms. Welch.

Again, questions from the panel for Ms. Welch?

DR. KIMBERLIN: This is Cecilia Kimberlin.

Jan, thank you very much for that very quick but thorough overview. I concur with many of the points, and all of the points that you made. I just have a question as I sit here. You didn't specifically address management control, and under that quality planning occurs resource allocation.

MS. WELCH: Right.

DR. KIMBERLIN: The kind of big picture of how well is our Quality System working. And I was just wondering if that was just so obvious

in your thinking, that management control really overrides all of these things, or should we specifically draw it out and address it perhaps later?

MS. WELCH: No, I think that's a good point. I think it was more in the interest of brevity, and I was trying to go to the parts that really affected manufacturing. But your point is absolutely there, because none of this will be successful. If the management with executive responsibility don't provide the resources, don't provide the time, the right way to do this, and the support, it will never be successful. So thank you for that. It's key.

MS. BLACKWOOD: This is Liz Blackwood from Industry.

Jan, just another thought. And I'm not sure exactly which element of the QSI this fits into, but it might be good to think about how our call centers are prepared to talk to hospitals, clinics, care providers, whether they're home care or what have you, to be able to let them know what would be an alternative device, what would be a competitive equivalent to keep the continuity going, especially on life-saving, life-sustaining glucose meters, that kind of thing that you've got to have every day, if you can't get strips, right? You can't get to the pharmacy or the pharmacy can't get their supplies.

So sometimes, as we know, these events affect certain parts of the world, and that same product, even though it's a competitor, we hate to do it, but we want our customers to be safe and happy. So could we think about having that kind of a script for our call centers?

MS. WELCH: So is that something that you have sort of -- you

would envision through your -- your call centers are generally part of your complaint handling system or --

MS. BLACKWOOD: And order processing.

MS. WELCH: Okay, all right, order processing as well.

MS. BLACKWOOD: Because we do that as a matter of planning for recalls, right?

MS. WELCH: Correct.

MS. BLACKWOOD: So when we know we're going to have a removal or a correction of a significant --

MS. WELCH: Right.

MS. BLACKWOOD: -- magnitude and put continuity for the hospitals or the clinics on hold, we know that we have to have a competitive backup or equivalent for them. So we have that prepared. Why couldn't we use that same thinking in the disaster situation?

MS. WELCH: Right. No, I agree with you. And I think this is something -- I think this is a great place where FDA and the industry can partner on this. And I think we did a pretty good job internally on nylon 12, because we were looking at this -- if this particular component had not been available, what would've happened, right? And so we have the ability to kind of look back and look at all of the industry, all of the products, and I think in certain circumstances, which these lend themselves to, we can partner with that information. But we all want our patients to have the right product and

have it available.

So I think that we can work, too, with our resources to get that information. If a manufacturer were to approach us and say oh my gosh, please help, we can mobilize and get that information as well.

MS. BLACKWOOD: Yeah, because I think just from, you know -- I mean, this sounds crazy to say, but just economically, you have to make certain calls about certain devices. So we have a blood testing business. When Sandy hit, the vice president of operations sat at my kitchen table because I happened to have Internet. She drove over to my house, and she got that place back up and running within two hours. We were able to go to the Red Cross and supply.

MS. WELCH: Right.

MS. BLACKWOOD: And then we had backup plans for the employees to be able to stay close to the facility. There's actually a dormitory. You know, we have a plan --

MS. WELCH: Right.

MS. BLACKWOOD: -- because we're the only game in town in that particular case, and it's blood supply. Would you do that for every single product? Probably not. So you might risk stratify --

MS. WELCH: Right.

MS. BLACKWOOD: -- the supply and the type of device, whether or not you'd offer competitive versus you've got to get back up and

running.

MS. WELCH: That's right. And as I said, this is something that you all may consider this afternoon, that if this manufacturer is the sole manufacturer and something were to happen, then they may have to have different mechanisms, you know, more robust mechanisms, that somebody who's -- okay, there are 50 people that make this device. So does that mean that they have to have a less robust -- so it depends on what it is and how critical. But maybe the recommendation is that there needs to be more of, as you said, a backup system and plan.

DR. CRANMER: This is Dave Cranmer.

Do you envision a point at which FDA issues a guidance document with some best or better practices in quality systems that address things like you mentioned with risk analysis? It's great to do it once. It's better if you do it continuously on a regular basis. It's really good if you do it when you recognize things change. Would that kind of a guidance document be something you would be interested and able to do?

MS. WELCH: Well, I don't think -- we obviously don't have an explicit guidance on that, but we do have those statements in other materials that we prepared. And a lot of this material we prepared, obviously, back in 1996-1997 as we were rolling out the reg. So I'd be very interested if that's one of your recommendations this afternoon, whether it's with respect to these extreme events or others that don't have the catastrophic impact. But

we do have those considerations in some of our other documents.

DR. ZABRANSKY: A couple other comments. The regs, when they were written in the '90s, didn't address -- or does address, I should say. Throughout, it implies record keeping, and if it's not written down, it didn't occur. So, now, are these hard copy records? Can we store them in the cloud, which was never thought of back in the '90s?

MS. WELCH: You're absolutely right. And we're finding that almost everything has moved to some electronic media, some type of electronic storage. So it's better in some ways so that manufacturers aren't going to end up with these storage roomfuls of wet records that are destroyed, but again have to plan for that. Where are these backups going to be located as well? So that has its pros and cons, too, but at least there aren't, as I said, these voluminous records that are wet and destroyed anymore.

MS. BLACKWOOD: I think, on the electronic side, there are so many regulations in the IT space around security, update sources, the HIPAA, the HCC, and Sarbanes-Oxley and so on, that our electronic data centers do have massive generators and backup chillers and all of that kind of thing. But truth be told, we still have a lot of paper. We do.

MS. WELCH: Okay.

MS. BLACKWOOD: Right?

MS. WELCH: All right.

MS. BLACKWOOD: And so that might be one of those exemptions where you say, well, do I have to revalidate everything because my paper validations were here? Not everybody's like that, but --

MS. WELCH: I agree, I agree. And I think that it's important that you don't have to go back and do all of this. But what's the subset of activities --

MS. BLACKWOOD: Right.

MS. WELCH: -- in any one of these parts of the quality system --

MS. BLACKWOOD: Right.

MS. WELCH: -- that need to be -- right, you move something --

MS. BLACKWOOD: What would be adequate to demonstrate?

MS. WELCH: That's right, what's the subset of activities? Absolutely.

DR. ZABRANSKY: I'd like to pose a question for Ms. Blackwood there. Earlier she mentioned something about if a company's product was not available, can you recommend another company where it might be available? Again, from my perspective in a clinical laboratory, if I was required or had to take on another product, I'd have to verify it and validate it according to CLIA and according to the College of American Pathologists' laboratory accreditation, which all takes time. Now, you know, can the

laboratories or can any user be exempt from that kind of re-verification of a product that they had not used before?

MS. BLACKWOOD: You mean in the hospital or in the clinic? That's a great question. That's a good question. I don't know the answer to that, but that's definitely outside of FDA's bailiwick, I would say.

MS. WELCH: Good.

MS. BLACKWOOD: Right?

(Laughter.)

MS. OLIVERA: Mary Olivera.

You discussed the fact that some of these medical devices are manufactured in places that they may have extreme heat and may be stored and transported in conditions that are not suitable for these medical devices. Perhaps there can be some guidance to manufacturers, in which they can have a visual indicator on those packages of the items that are heat sensitive, so when it gets to the end user, you can visually see that the package is still good and is not or has not been exposed to any of those conditions.

MS. WELCH: That's a great idea. So the regulation would -- that's sort of a neat kind of storage requirement, or something like that, that again, the manufacturer could design that in as a design requirement and then to verify that as part of their design verification along the way, that that packaging, that that indicator, sensor, or whatever works. So that's a great tool that they could implement and design into that whole chain of the

device. Yeah, that's a great idea.

MS. OLIVERA: Correct. Thank you.

DR. ZABRANSKY: I would ask that the Committee keep some of these thoughts in mind as they go through the questions again this afternoon. You know, should these be recommendations to the FDA about, I hate to say, changing the regs or maybe a guidance document, as Dr. Cranmer mentioned? Again, if you have more questions related to this, this again can be addressed later on.

Again, thank you.

MS. WELCH: All right, thank you very much.

DR. ZABRANSKY: We are now kind of ahead of schedule by about a good half hour or more. We can take a break now. Instead of a 15-minute break, let's talk a half-hour break, if you want to get yourself a cup of coffee, press your shoelaces or whatever you do during the breaks. Okay. And we'll resume, then, at what, 9:45, okay?

(Off the record.)

(On the record.)

DR. ZABRANSKY: I'd like to call the meeting back to order.

We're now going to proceed with the FDA's third presentation. And, again, the questions that we may have for the speaker will be only from the panel, not from the public, at this time.

We're going to now hear from Captain Kimberly Lewandowski-

Walker on the compliance program and the challenges of extreme weather.

Captain Lewandowski-Walker, welcome. Thank you.

CAPT LEWANDOWSKI-WALKER: Thank you very much. I'm very happy to be here speaking to you, and I'm very excited that CDRH asked me to speak, as well.

Just a little bit about myself. I am a commissioned officer with the U.S. Public Health Service. My doctorate degree is in optometry, and I have a master's degree in human services. I actually started my government career back in 1997 with Indian Health Service, so I was actually a clinician that worked out on Indian reservations, primarily in the Southwest. And I do maintain my clinical competency even today. So I like to a keep a hand in the clinical aspect as a user of medical devices, primarily ophthalmic devices, but a user as well as being on the regulatory side, as well. I am with the Office of Regulatory Affairs, or ORA. I'm one of the medical device national experts, and I work out of the Office of Medical Products and Tobacco Operations.

I'm going to tell you a little bit about the way FDA is set up, for those of you who don't know. Again, I'm with the Office of Regulatory Affairs, or ORA. ORA's headquarters is in Silver Spring. Really, ORA is kind of like the field branch of FDA. So we have the five product centers, and then we have the inspectional and investigational arm as well, which is what I am in.

In terms of ORA, what we do is we really support the five product centers. We conduct inspections, investigations, sample collections.

We collect import samples, and we have laboratories, as well, that are in our purview. We're organized into five regional U.S. offices. Within those five regions we have 20 district offices. We also have approximately 150 resident posts and border stations as well. And we also have 13 laboratories. Approximately 85% of ORA's employees work out of these five regional offices, resident posts, laboratories, and the district offices. Most of you are familiar, then, with the Center for Devices and Radiological Health, or CDRH. Again, the headquarters is here in Silver Spring.

We also have staff posted in several countries, which are listed on the slide here. We have FDA staff also in the U.S. Virgin Islands, in Puerto Rico, and in all 50 states except for Wyoming.

A little bit about our premarket device classes. Devices are classified using a risk-based approach. Class I devices are the lowest-risk devices. They're subject to what's called general controls. Most of the Class I devices are exempt from premarket notification, or you may have heard it referred to as a 510(k). Class I devices, just some examples, are things like simple surgical instruments, simple surgical retractors, screwdrivers, that kind of thing, tongue depressors. So these are simple devices. They are subject to general controls, which means that most of them are subject to good manufacturing practices, which fall under the Quality System regulation, as Jan spoke to you about. They also fall under provisions for things like record keeping, device notification, adulteration, misbranding, those sections of the

FD&C Act. Those are all parts of what we call general controls.

Our next risk classification is the Class II. These are moderate-risk devices, and this is honestly a huge diversity of devices in this Class II category. Everything from daily wear contact lenses to MRI machines are considered to be Class II. They are moderate risk. In addition to general controls, which is GMP requirements, requirements for not adulterating or misbranding the devices and things like that, there can also be special controls, as well, associated with these devices. Special controls can be things like mandatory performance standards, special labeling requirements, or maybe requirements for postmarket surveillance that the Agency would impose on these types of devices.

Class III devices are our highest-risk types of devices. These typically require a premarket approval, although some of these are still under 510(k). Class III devices, just to give you some examples, are things like our pacemakers, our implantable cardioverter defibrillators, silicone breast implants. So if they're a higher-risk device, typically it's a Class III.

The premarket device classes really encompass about 1700 product types. So CDRH and those of us in the field who do medical device inspections really are responsible for a wide variety of devices.

Our authority to conduct inspections is found under Section 704(a) of the Food, Drug, and Cosmetic Act. This is actually language that appears on our notices of inspection, or our Form FDA 482s, that we issue to

firms that we inspect.

It essentially says that we are designated by the Secretary, when we present our credentials and a written notice, to enter, at reasonable times, any factories, warehouses, or establishments in which devices are manufactured, processed, packed, or held, for introduction into interstate commerce or after introduction. We can also enter any vehicle used to transport or hold those devices. And we can inspect, at reasonable times and at reasonable limits and a reasonable manner, those factories, warehouses, establishments, or vehicles.

When we establish our inspectional priorities, we do several things. One of the things that we do first a lot of times is we search the FDA's registration database to identify medical device manufacturers. Medical device manufacturers are required to submit a registration to FDA. The reason that they do this is we need to know who's out there. They're also required to most of the time, when they submit that registration, to also submit a device listing. So the device listing basically says, for a particular manufacturer, what devices do they either manufacture or design, or if they're an initial importer into the United States.

So when we start to think about what firms we want to inspect for that year, we're going to search the registration database, find out who's out there, and we also want to find out what they make.

When we establish those inspectional priorities, we really try to

prioritize based on several things, one of which is the risk of the device. So it just makes sense that we want to try to get to those firms that make the high-risk devices, like the pacemakers, the implantable defibrillators, before we go to the tongue depressor place. Now, if the tongue depressor place is somehow hurting people, then fine, we'll go there. But we really try to prioritize the resources we have towards the higher-risk devices.

We also look at the inspectional history of the manufacturer. So we'll look at how was the previous inspection classified? Was it classified as a violative inspection? If so, we'll try to go back to those firms before we go back to firms that were classified as non-violative.

We also look at the date of the last inspection. So if we have a firm that was inspected just last year, we'll try to go to firms that we haven't been to in maybe over two years.

We also look to see if maybe there's new device types out there or some new firms. Maybe there's a firm out there who's making a new device using some sort of novel technology that there's not a lot of data out there. So we'll try to inspect those places as well.

Another way that we establish our inspectional priorities is through this newer program. This is the voluntary ISO 13485 2003 report submission pilot program. This actually came on board in June of 2012, and what this does is this allows medical device firms who have been audited against ISO 13485 to submit those reports voluntarily to CDRH, and we'll use

those reports to make some sort of risk-based decision as to who we're going to visit. So ISO 13485 is very similar in a lot of respects to the FDA Quality System regulation. It's essentially the international standard for medical device manufacturers, very commonly used outside of the U.S.

The voluntary audit report submission program is part of the Food and Drug Administration Amendments Act of 2007, which mandated that we would accept the voluntary submission of these ISO reports for the purpose of setting risk-based inspectional priorities. So this is a voluntary program. The firms, if they meet certain criteria, can voluntarily submit their ISO 13485 report to CDRH, who will then classify the report.

So why do we accept these reports when we have our own Quality System regulation that we inspect to? Really, it's for risk-based planning and the efficient use of our limited inspectional resources. As I said, ISO 13485 is the international quality management system standard for medical device firms that is used around the world. Many more audits are performed against ISO 13485 than we at FDA are able to personally perform, inspecting to 21 C.F.R. 820. So ISO 13485 is used internationally. Lots of firms are audited to it.

There are some things in the Quality System regulation that are actually quite a bit more proscriptive, in terms of things like complaint handling, than ISO 13485 is. But essentially 13485 is largely harmonized with the Quality System regulation.

A little bit about the -- I'll just back up one slide here. Pardon me. So a little bit more about why we accept these. If you think about if we have two firms, okay, and we've not been to either one, ever, for example, so we have no inspectional history. If we're going to set some risk-based priorities, if we have a voluntarily submitted ISO 13485 report from Firm A and we have nothing from Firm B, some information is better than no information. So if we get one of these voluntarily submitted reports and it's classified as non-violative by CDRH, the firm actually gets a one-year, sort of, extension on when we go to an FDA inspection. We would try to give our inspectional resources to the firm that hasn't submitted a voluntary report. So, again, some information is better than no information.

These voluntary reports, at this particular time, are not a replacement for an FDA inspection. It is not in lieu of an FDA inspection. It simply gives FDA more information as to does this firm have some sort of processes in place? Have they been audited by someone versus the firm that we have no information about, other than what they submitted in their registrations, listings, and perhaps their 510(k)s?

I'm going to talk to you a little bit about our compliance program. For medical devices, it's Compliance Program 7382.845, inspection of medical device manufacturers. This is really the tool that we use when we're doing inspections or sample collections or investigational-type work to assess if the medical device manufacturers that we're responsible for are

meeting their requirements under the Food, Drug and Cosmetic Act and the other regulations. Part III of the compliance program discusses inspectional strategies.

A little bit about the Quality System Inspectional Technique. This is one of our main tools that the FDA investigators use when they're performing inspections. It starts by looking first kind of at the firm's systems and procedures and then drilling down into each one of those subsystems, which I'll talk about in a little bit, to see if their firm is actually following their procedures and if their systems that they have in place are adequate. It was developed by FDA and introduced in 1999 and it helps us conduct an efficient and effective inspection, focusing on key elements of a firm's Quality System.

Within the Quality System inspectional technique, it's divided up into seven subsystems. The primary subsystems are management, Corrective and Preventive Actions, design controls, and production and process controls. These are referred to as the four main subsystems. Things like materials controls, records and document controls and equipment controls are inspected as linkages from the four primary subsystems.

When the Quality System Inspectional Technique was validated back in 1999, it was validated to have the inspections conducted in a particular order. So if we're going to do a four-subsystem inspection, we start with management. The next is design, followed by Corrective and Preventive Actions, and then production and process controls. So that's the way the

system was validated in 1999.

Our compliance program also allows for the order of management, Corrective and Preventive Actions, then design controls, and then production and process controls. So there's a couple ways we can do that.

The compliance program outlines different types of inspections and different inspectional levels that we'll do. The first one is a Level 1 inspection, or an abbreviated inspection. It involves the investigators inspecting the Corrective and Preventive Action subsystem, plus either design or production and process controls. Typically a Level 1 inspection is performed when we have some inspectional history on the firm and that inspectional history is non-violative.

So rather than doing a lengthy four-subsystem inspection every time we go in there, if we've done a baseline inspection, which is the Level 2, the next inspection we might choose to do is an abbreviated. So we always look at Corrective and Preventive Actions and then, depending on what we're seeing in the Corrective and Preventive Actions, we'll either choose design or the production and process control subsystem.

Alternatively, if there's a series of these Level 1 inspections that are done, we might say, well, this time we're going to look at design, and next time we'll look at production and process controls.

Level 2 inspections are baseline inspections. This is when all

four major subsystems are inspected. So again that's management, design controls, Corrective and Preventive Actions, and production and process controls. We typically do these as initial inspections. So if we have no inspectional history on the firm, very often we'll do a baseline inspection. The foreign inspections that we do -- so if we go to Belgium, for example, and do an inspection of a manufacturer in Belgium that sends products to the United States, we'll do a baseline inspection there as well.

Level 3 inspections are compliance follow-up inspections. These are typically performed if the inspection was found to be violative in some manner. So either a Level 1 or a Level 2 inspection was violative. We'll go back in and we'll assess. Has the firm made corrections? Are there continuing problems? Those are considered to be compliance follow-ups. We might use some elements of the QSIT guide in these types of inspections, but we're really looking at seeing if the firm is making progress towards correcting problems or if there are new problems that are arising.

Addressing high-risk devices in the compliance program, I already talked to you about the way we prioritize in the premarket side with Class I's, II's, and III's. The compliance program also has some information on high-risk devices. So these can be things that are identified through special assignment from CDRH. Maybe it's a Class II device but it has a high frequency of recalls and medical device reports, so that might be considered a higher-risk device in terms of the compliance program.

We also look at devices that are driven by software or those that have some sort of novel technology, because both of these types of devices can be subject to some poorly controlled modifications. Software is notorious for this. That could affect their safety and efficacy. Or if it's a novel technology, there's just not a lot of data out there sometimes about it. Maybe it's a brand-new device, so something we've never seen before.

In the compliance program, I mentioned to you that the QSIT inspection technique was validated using -- it's always production and process controls last. And there's really a reason for that; the selection of manufacturing processes for inspectional coverage. We look at a number of things when we're doing the inspection. One of them is we need to know if there's any Corrective or Preventive Action indicators of a process problem, because if there is, then we would want to focus on that particular process.

Maybe there's a process used to manufacture a higher-risk product or processes that have a high risk of causing the actual device to fail, processes that require validation, maybe it's a new process for that particular manufacturer, or maybe it's used to manufacture multiple products. So we really try to make a judicious selection of which manufacturing process we're going to look at during our inspections, based on what we're seeing in Corrective and Preventive Action subsystem and the design subsystem as well.

The compliance program also tells us it's important to

thoroughly cover purchasing controls, to include outsource processes as a QSIT linkage whenever production and process controls are covered. So as Jan mentioned to you, back in 1996, when the Quality System regulation was promulgated, there wasn't the degree of outsourcing that there is today. So our compliance program tells us we really need to pay attention to the purchasing controls.

I've personally been to many device manufacturers where it's the finished device manufacturer, and you go there and there's not much to see, other than a building with offices, because they contract so many other processes out. So we need to look at that in our inspections. And we also need to document that in the establishment inspection report, especially if they contract out a sterilization process or the manufacture of significant components, subassemblies, or processes.

So when I talked to you about the Level 1, Level 2, and Level 3 types of inspections, so the abbreviated, the baseline, and the compliance follow-up, those are more or less the routine types of inspections on that third bullet point there.

We also have other types of inspections that we perform. We have for-cause inspections. So maybe we got some complaints from consumers that said, hey, maybe we need to go take a look at this firm. Maybe there's a trend in medical device reports, that people are being injured or killed by a particular type of device. Maybe there's an article in the

press. A lot of our medical journals will write articles comparing failure rates of different types of devices, and if we're made aware of some of those articles, we might choose to do a for-cause inspection at the firm as well.

It can also be something received in our submissions that might prompt us to go ahead and do an inspection of that firm for-cause. A lot of the for-cause inspections, we might again use elements of the QSIT guide, but we're really driven to whatever the event is that is prompting the inspection or where the quality problems are in those cases.

We also do preapproval and postmarket inspections. So this is for, typically, our Class III devices. We'll go in before an original PMA is approved and do an inspection, or maybe after a supplement. We also audit clinical studies as part of our biomedical research monitoring program, and we have our compliance follow-ups as well. So if a firm is issued something like a warning letter or if they're under a consent decree or something like that, we'll have to do compliance follow-ups as well. We also have risk-based inspections.

A little bit more about for-cause inspections. These are usually initiated at the request of CDRH through ORA headquarters, or it can be the result of some sort of regional or district directive. Again, as I told you before, these are dictated by the source of the information. So if we know that there's a lot of medical device reports being submitted for a particular device made by a particular firm that is injuring people in a particular way,

that might be the focus of that type of inspection. Again, we might use some elements of the Quality System Inspectional Technique, but these types of inspections are usually more in depth in those areas that are particularly problematic, or what led to whatever the for-cause is, than a typical QSIT inspection.

Again, we usually give inspectional guidance with these types of for-cause inspections. So typically what will happen is CDRH will issue an assignment, or from headquarters, and we'll follow these assignments as we're going out there. We're really looking at the quality problems in these cases, and we're trying to trace the underlying cause, ensuring that appropriate corrections and corrective actions are initiated by the firm.

CDRH also has a risk-based work plan. So these types of inspections are initiated at the request of CDRH. They're focused on whatever, maybe, the Center found through some sort of analysis. And, again, these are kind of like the for-cause. They differ a little bit from the typical QSIT approach. They're typically more in depth in a particular area than a typical QSIT inspection would be. We're normally issued an assignment for these risk-based work plan inspections. So we'll cover the areas listed specifically in the assignment, using elements of the QSIT guide as appropriate.

So when we talk about extreme weather considerations, because that's why we're here, when we think about well, okay, can you

spend a lot of time talking about all of these different types of inspections and risk based and for-cause and Levels 1, 2, 3, honestly, if there's an extreme weather event, it does not matter what we call these types of inspections. Because if it's risk based, for-cause, or just assigned to us as a normal inspection, if there's been an extreme weather event, we're going to look at a lot of the same things.

So one of the things we're going to look at is what process was affected during the extreme weather event. And I know Jan addressed storage and shipping and validated processes. We're also going to look at processes performed by suppliers when we go out there and do that. And we're going to want to know if appropriate Corrective or Preventive Action was taken as a result of the extreme weather event.

We're also going to look at supply products because there is a lot of outsourcing now. Firms don't do everything in house like maybe they used to do 20 years ago. And one of the things we have to consider is, while our finished device manufacturer may not physically be located in the area of an extreme weather event, perhaps one of their critical suppliers is. And according to the Quality System regulation, the finished device manufacturer is responsible for the activities of their supplier. Under the act, FDA can go in and inspect component manufacturers, okay, but they're not subject to the Quality System regulation.

So we typically don't do a lot of component manufacturer

inspections. We really rely on the finished device manufacturer, under purchasing controls, to control their suppliers. So we'll want to know how that finished device manufacturer is controlling that supplier to ensure that the products or services that the finished device manufacturer receives are going to meet specified requirements.

So our priorities after an extreme weather event. I would like to say that if an extreme weather event happens, that we're out there inspecting all of these medical device firms. But the reality is, as a public health agency, one of the first things after Hurricane Sandy or Katrina, or any of these events, is food and water. You know, a lot of the inspectional -- the resources that ORA has in the districts, we're going to go out there and make sure that food and water is safe. That's the number one priority. Because if you think about just a public health perspective, food and water in a particular region is going to affect everyone. Okay, medical devices don't typically affect everyone in a particular area. So the first priority is, if there's a disaster of some sort, is food and water safe?

The next thing we'll do is we'll look at the pharmaceuticals. So if there's a pharmaceutical distribution center or a warehouse, we might pay them a visit after an extreme weather event to make sure that the pharmaceuticals that they're holding haven't been contaminated in some fashion and that they're safe to distribute. The fact is, a lot of people -- maybe a lot more people use pharmaceuticals than actually are users of

medical devices.

So after we cover those two types of areas, then, if there are resources available, we'll cover some of the commodity areas, including medical devices. But, again, I can't stress enough, after one of these events, the first priority is, is food and water in the area safe?

We really rely heavily on our medical device firms to take into consideration, if they have been involved in an extreme weather event, that they're kind of doing what they need to internally to make sure that the products they produce or the supply products that they receive are safe and meeting their specifications.

If we do an inspection and it is found to be violative, we have several avenues we can go down. We have everything from an administrative action, such as a warning letter, all the way to things like seizures and injunctions. So these are some of our regulatory strategies that we have. This isn't just for extreme weather events, but this is for any type of inspectional activity that we do. We have these options if a firm is violative and we have tried to bring them into compliance with no success.

Just in summary, our medical device manufacturers need some awareness of FDA's organization, especially the Center for Devices and Radiological Health and then the Office of Regulatory Affairs as well.

We have established a risk-based product class scheme, so Classes I, II, and III. And as I mentioned before, our product classifications

encompass over 1700 general device types.

I think I stressed enough that really, as an ORA person, I know that our inspectional activities after extreme weather events, the first thing is, is food and water in the area safe?

So it really is imperative that device manufacturers plan for these types of extreme weather events where there are possible disruptions to their supply chain, if they know they have a supplier that's located in an area that might be more subject to some of these extreme weather events.

If our device manufacturers have questions regarding what activities they should take after an extreme weather event, they can contact their local district office for assistance.

I have some references listed here on this slide. This shows where you can find our Compliance Program, the Guide to Inspections of Quality Systems, and some other things.

MS. BLACKWOOD: Okay to ask a question?

CAPT LEWANDOWSKI-WALKER: Yes.

MS. BLACKWOOD: Oh, good.

DR. ZABRANSKY: Oh, thank you.

Go ahead, you have a question. I'm sorry.

MS. BLACKWOOD: I don't mean to interrupt you. Go ahead with your --

DR. ZABRANSKY: No.

MS. BLACKWOOD: Okay.

DR. ZABRANSKY: Go ahead.

MS. BLACKWOOD: Liz Blackwood again, representing Industry.

One of the things you mentioned in approach in manufacturing, in terms of how you do inspections, is based on processes that yield high-risk products.

CAPT LEWANDOWSKI-WALKER: Yes.

MS. BLACKWOOD: So let's kind of play this forward to this afternoon, and we're having conversations about -- we've kind of focused on the areas that we know are generally impacted, storage, preservation, distribution channels, production controls, and so forth, suppliers.

Would we consider starting with a list of what we'll call critical devices, maybe it's Class III, maybe it's Class III plus some small number of Class II, where we would want to require certain things that are preventive in nature versus anticipating that we would expect manufacturers to have preventive actions in all types of devices?

And then on Class II and Class I we have corrective requirements like inspection and test and monitoring and that type of thing. Do you follow my logic?

CAPT LEWANDOWSKI-WALKER: I do. One of the things, as I mentioned, there are 1700 different product classifications. You know, if we're at the tongue depressor place, are we going to require them to have

such a plan for an extreme weather event? We have to look at some of the risks of making some of these devices.

And while there's nothing prescriptive in the regulations that says these classifications or particular products need to take into consideration an extreme weather event, I think Jan touched really nicely on the fact that device manufacturers are required, if they're subject to design controls -- so most of the Class II's and all of the Class III's -- to say, okay, we're going to do a risk analysis, and what are potential ways that our devices could be misused, for example.

And then, you know, hopefully something that can come out of a panel meeting like this is maybe device manufacturers can start thinking more about those extreme weather events before they actually happen. But there's nothing in the regulation or in the premarket side that would require them at this point to really say, well, what happens in the event of an extreme weather event?

Some of the hospital-type equipment, you know, we'll have requirements for backup batteries and things like that. But in terms of just general product classifications, a lot of these low-risk devices, we're not seeing this being a huge problem. But I think our higher-risk device manufacturers should really consider how their devices are being used and take into consideration some of these extreme weather events.

DR. ZABRANSKY: Dr. Cranmer.

DR. CRANMER: Dave Cranmer.

In listening to your presentation, one of the things that occurred to me is that your resources for inspection are constrained like every other government agency --

CAPT LEWANDOWSKI-WALKER: Yes.

DR. CRANMER: -- to do whatever it is they do. Is there an opportunity and a legal authority for you to deputize somebody else to do inspections on your behalf in extreme events like this?

CAPT LEWANDOWSKI-WALKER: We actually do have something called an accredited persons program, and this is a program that is still active, where third-party auditors can go through a process where they can do inspections on FDA's behalf. So there's a process that they need to go through. There's typically an application process and then some on-site audits that they have to do, where someone like myself would watch them do audits and see if they're doing things the way that FDA would prescribe them to be done. So there are programs like that --

DR. CRANMER: Okay.

CAPT LEWANDOWSKI-WALKER: -- where third parties can do inspections on our behalf.

DR. CRANMER: Okay. It occurs to me, since MEP has a physical presence in all 50 states and Puerto Rico, that might be a linkage we can make that might help both of us down the road.

CAPT LEWANDOWSKI-WALKER: There's also two states that have what you might call deputized investigators.

DR. CRANMER: Um-hum.

CAPT LEWANDOWSKI-WALKER: Texas and California have folks that can do inspections on FDA's behalf in the medical device arena. In the food and other areas, we rely heavily on the state inspectors to do a percentage of those types of inspections for us as well.

DR. CRANMER: And the question that I know will get me in trouble with my own agency, but I'm going to ask it anyway --

CAPT LEWANDOWSKI-WALKER: Go ahead.

DR. CRANMER: -- as you were talking, I think the way you posed the question was, why does FDA accept ISO 13485 reports when we have 21 C.F.R. 820? My question is the exact opposite of that, is why do we have both? When there's an accepted international standard, why does FDA have a separate one?

CAPT LEWANDOWSKI-WALKER: Well, part of that is some of FDA's requirements, particularly for complaint handling, are more prescriptive than are what's required in that standard. So when the Quality System regulation was being promulgated in 1996, I believe ISO 90001 was still the quality management system standard. So at the time that the regulation was promulgated, 13485, to my knowledge, wasn't in existence.

But there are differences between the two. And I'm also a lead

auditor for ISO 13485. I took the course and I know there are differences. I think our regulation requires more in terms of proceduralizing several things. And, again, the complaint handling requirements are much more prescriptive, which is really actually very important that we have those prescriptive complaint handling requirements, because one of the ways that we do prioritize some of our inspectional activity is through the submission of medical device reports.

So if we don't get appropriate -- if the firms aren't getting appropriate information from complaint handling to make good decisions as to what needs to be reported to the Agency in terms of serious injuries, for example, then we really can't prioritize those inspectional resources as well.

DR. CRANMER: Okay. Because it occurs to me -- and the last thing I want to suggest is that somebody rewrite regulations, because I know what a royal pain that is on a good day. But if that were to be part of the process, would you potentially say, generally, we accept ISO 13485 with these small additions that cover the things that are important to you in that extra reporting and complaint handling?

CAPT LEWANDOWSKI-WALKER: I would answer your question this way. There's a lot of effort being made to harmonize the Quality System regulation and 13485. The fact is ISO 13485 probably gets updated, or at least thought about getting updated, more than the Quality System regulation does. But there are efforts to harmonize those two, because one

of the things we don't want is firms that are located or in maybe foreign countries or that sell to outside the U.S., to have to try to comply with requirements that are conflicting. So there is a lot of effort made to harmonize requirements between FDA and the rest of the world.

DR. KIMBERLIN: Cecilia Kimberlin, Industry Representative.

I'm aware that the Agency has some efforts going on to identify and be more proactive on medical product shortages. So I think it started on the drug side, but I also saw some information that on the device side, the Agency is working with industry to try to be preemptive and start identifying what kinds of products, if there were shortages, would create a critical public health issue.

So how does that effort, although it's, I think, very recent, how would that effort tie into this kind of activity, in terms of would it help you prioritize firms? Would it help us to understand, as you said -- and I'm building on what Liz said -- that not everyone would have the same level of risk management because there wouldn't be the same criticality in a short supply situation?

CAPT LEWANDOWSKI-WALKER: Right. To my understanding, the shortage issue that is being looked at, that's a CDRH initiative, and I'm with ORA. So one of the things that I think, you know, may be something for the panel to think about this afternoon is, if there are devices that are identified as critical or that there's maybe not a lot of manufacturers out

there, that firms should, as you said, think about if my plant is damaged or I can't get my product out, are there other products that, maybe in this emergency situation, that as a manufacturer you might know about and say, sorry, we can't send you what we have, but maybe you can call this other firm because they have something similar?

DR. ZABRANSKY: You made the reference to the ISO, and Dr. Cranmer did. We're talking about manufacturers that are overseas, foreign, that are either providing the raw materials or components that are now put together in the United States. Is it that you rely strictly on the ISO regulations dealing with those?

CAPT LEWANDOWSKI-WALKER: Well, component manufacturers are not subject to the Quality System regulation. According to the Quality System regulation, the finished device manufacturer is responsible for the activities of those suppliers. So we would audit the finished -- inspect the finished device manufacturer and assess what type of controls they have over that supplier, including how they evaluated that supplier to assure that that supplier will produce quality product, and things like acceptance activities performed by the finished device manufacturer.

We don't really rely on an international standard in most cases to monitor suppliers or component manufacturers in most cases. Exceptions might be things like contact sterilizers, for example. But we require those firms to follow 820, 21 C.F.R. 820, and to register as well.

But in terms of is there some sort of blanket standard for these places that are component manufacturers or just maybe making some sort of subassembly? No.

MS. BLACKWOOD: One thing to add to that from a manufacturer's standpoint -- this is Liz Blackwood, Industry Representative -- is that we're finding, actually the further east you go, the more important it is to understand the chain of custody of the materials that you're putting into your products, and particularly in the area of electronics, you know, with trying to get lead out of devices, other than X-ray, which obviously needs it.

So realize sometimes that there are supplies that are tainted, and if we don't have a strong handle on the chain of custody for that supply, they may outsource it if, for example, their supply is running low or their supply is damaged or exhausted through some transportation gap and that type of thing.

So I was thinking about this in terms of the extreme weather conditions and that is, if we had -- and this doesn't even feel to me like it's outside of the QSR. You really should know where your products are coming from and that they came directly from the source that you qualified, right? So I think the chain of custody around those suppliers and then being in touch with them to know if they did have extreme weather conditions, what did they do, similar to how FDA holds us accountable.

We as the manufacturers are very much aware that we're

accountable for that, and that's a way that we contract, I would say. So through our quality agreements in the supplier quality agreement, we would say you have to notify us of changes to processes, materials, sub-suppliers, blah, blah, blah, and extreme conditions would be a perfect place to put that.

DR. ARMSTRONG: Brenda Armstrong.

I have a question just in terms of jurisdiction. And as much as you look at what goes in on the front end, in the case of a disaster where there are materials that are deemed now not usable, where does the FDA's oversight end with respect to disposal of those devices?

CAPT LEWANDOWSKI-WALKER: So is your question if there were -- when you say products, are you referring to finished devices?

DR. ARMSTRONG: Yes. Say, for instance, in the case of Katrina --

CAPT LEWANDOWSKI-WALKER: Um-hum.

DR. ARMSTRONG: -- where whole hospitals were essentially just devastated and there were devices that you had said were okay but now are not usable or contaminated or whatever. Where does your jurisdiction end and there is another jurisdiction that takes over?

CAPT LEWANDOWSKI-WALKER: Well, typically, in our normal activities, we're really looking at the manufacturers. Under the act, we would have some jurisdiction at places where devices are held, and I think hospitals would fall under that particular category. But truthfully, you know, we would

probably make a visit to some of those hospitals, but would we demand that they destroy something? I don't know that we would take it that far. But we would certainly provide them assistance. We could help have some boots on the ground per se and guiding the hospitals, but I just don't think we would demand that they destroy something. Maybe some of my other panel -- our other CDRH folks can give an example as well.

MS. WELCH: This is Jan Welch.

I would say that in those scenarios, we would be looking to work with the local health departments, whether it's the city or whether it's the state, to assess the risk. And then they may have tools and regulatory mechanisms that are beyond our scope.

CAPT LEWANDOWSKI-WALKER: Yeah, that would be the local departments have embargo authority, for example, that we don't have. So I think that's a great point. You know, we might want to work with some of the local health authorities to see what's going on at some of these hospitals, if we do feel like they're continuing to use devices that maybe are probably not acceptable due to some sort of extreme weather event.

DR. KIMBERLIN: May I ask a follow-up question or a comment to Jan and Kim?

So where would corrections and removals, the 806 part, fall into this in terms of -- you know, I would assume you're working with manufacturers. You've identified product now that's suspect and you have

information that it can no longer be used. Wouldn't there be an interface there as well?

MS. WELCH: So this is Jan Welch.

Yes, and I think it kind of goes to the interesting question that you asked. It's about this jurisdiction and who's got it last. And Kim talked about being held and being held in a hospital, but I sort of pose that back to you and Liz as manufacturers. It's at what point have you considered that product sold and distributed, and where do you work that into sort of your Corrective and Preventive Action system, working with your customers in terms of expectations? I mean, would they be filing a complaint back to you or the like? I mean, you didn't cause the problem. But then how do you both work together to decide is an 806 filing appropriate? It may not be, it may not be.

MS. BLACKWOOD: I would say, in reality, you may never know that the defective product was as a result of the extreme conditions, so you would replace it, investigate it, and determine if you needed to do corrections and removals. They may not ever tell us. Well, the lighting conditions weren't right or the heat was up in this room for X period of time and now they've embrittled, you know, it's embrittled the catheter. So we may never know and we may not -- we don't certainly have something proactive that says let's go see all of our customers to see do they have enough product, maybe? Or if they call us we might go in, right? And once

they contact us, we may never know.

DR. ARMSTRONG: So that's an assumption of good faith.

MS. BLACKWOOD: Yes, we do that a lot.

DR. ZABRANSKY: Does your office handle intravenous products as well as blood products that may be contaminated, or is that under another?

CAPT LEWANDOWSKI-WALKER: If it's considered to be a device, yes. If it's a drug, then that would be ORA. We're still the inspectional arm, let's say, of FDA. So we have inspectors or investigators that go out and do drug inspections as well.

DR. ZABRANSKY: Well, the reason I asked the question is because a scenario that I was involved with a number of years ago was an organism that caused five deaths in an institution. It was an unusual organism, and we called in through the state government to CDC, who did the inspection. Now, CDC is under the jurisdiction of HHS. So they determined that the contaminated IV fluid came from a specific plant that produced it. Now, where does your office get involved there?

CAPT LEWANDOWSKI-WALKER: If we were made aware that a scenario like that happened, we would certainly probably go to that manufacturer and try to determine, you know, what caused this, what may have failed in the firm's processes, and what the firm either is doing about the problem or should have done about the problem.

DR. ZABRANSKY: Well, CDC did all of the investigative work, and they actually determined what it was. It was related to the cooling fluid --

CAPT LEWANDOWSKI-WALKER: Um-hum.

DR. ZABRANSKY: -- that cooled these high-pressure sterilizers, and the plant was shut down completely.

Well, thank you very, very much, CAPT Lewandowski-Walker.

CAPT LEWANDOWSKI-WALKER: Thank you.

DR. ZABRANSKY: Any other questions?

(No response.)

DR. ZABRANSKY: Okay, thank you.

Again, the issues that have been brought up during this last presentation we can revisit these later on, so do keep them in mind for our further discussion this afternoon.

At this time we're going to have the FDA read some questions to us that we're going to be posing or trying to address this afternoon, and we're going to have Jennifer do this again.

Thank you.

DR. KELLY: Thank you. This is going to be a preview of the questions to the Committee for discussion this afternoon, in light of the current topic of extreme weather events and similar events, current successful practices for the medical device industry and the Agency, and

hopefully identify future steps for both the industry and the Agency to advance and better protect and promote the public health.

So Question 1. How should industry address extreme weather conditions during the device design process?

Question 2. How might Production and Process Controls from the Quality System regulation best be applied to ensure the safety and quality of medical devices that are affected by extreme weather events?

Question 3. How can Environmental Controls be applied to device production, transport, and storage to ensure that products remain safe and effective during and after an extreme weather event?

Question 4. How can Purchasing Controls be optimized by manufacturers to prepare for the event that component manufacturers may be affected by extreme weather?

Question 5. How can manufacturers utilize the Corrective and Preventive Action paradigm to effectively re-establish production after experiencing an extreme weather event?

Question 6. What additional steps or successful practices might firms take to maintain and monitor the quality of products or mitigate damage to products from extreme weather events during storage or shipping?

Question 7. What should firms consider with respect to their Quality System after an extreme weather event in order to be proactive for

future events?

Question 8. Are there elements of the firm's Quality System that FDA should highlight in inspections of manufacturers following extreme weather events?

Question 9. What is the appropriate balance of manufacturers' resources and staff time in anticipating and preparing for risks of Extreme Weather events?

And finally Question 10. Are there other recommendations for the FDA in light of extreme weather events?

DR. ZABRANSKY: At this time, obviously there's a lot of overlap between some of these questions, and at the same time some of them are grouped or related. I'd like to just have some general discussion, not about any specific question, but in general, following some of the discussions we had this morning, again reiterating this so that we can further address these questions later on this afternoon. So I'll just open it up for comments from the Committee.

DR. CRANMER: This is Dave Cranmer.

I'm actually going to tackle the first one because it seems to me, in that design phase, the way the technologies around computer simulation and modeling are going, that's a huge opportunity to explore more extremes of behavior without having to make physical devices and test them. So that might be an area that's worth looking at more carefully.

In theory, it's a cheaper option, but in practice, I don't know that it is as inexpensive, especially as you get to smaller sizes of companies. But I think it's worth looking at to see how that technology might be used to explore some of the robustness of the design analysis.

DR. KIMBERLIN: This is Cecelia Kimberlin, Industry Representative.

I agree, David, and I think that even in spite of that, let's just say industry did that perfectly. When there's a disaster -- for example, Liz and I have been through some of these in our industry experience, the tsunami effect, Sandy, hurricane. I mean, it's still a reality. You have to stop and assess. What you're suggesting where that helps us in industry is to have the data available to make better decisions. Do we have data to support extreme temperature? Do we have data to support outside of spec ranges, like Jan talked about?

But one of the things we might want to consider this afternoon in our further discussion is other areas for industry to require disaster recovery planning. Liz touched on it a bit as another Industry Representative, in terms of our enterprise systems. We look at it through the environmental side. We have requirements there to meet as industry.

So are there things that other agencies and other types of areas of our companies are working on that we could learn from and benefit from their best practices?

MS. BLACKWOOD: I can make maybe a general comment. I think that as Jan went through the QSR and starting with design being the foundation, I think the elements are there today in order for us to leverage the QSR from the standpoint of design, manufacturing, Corrective and Preventive Action, or postmarket processes and so forth.

I do think that there's probably some opportunity in the area of preservation during storage and transportation that could be an opportunity for us as a community. I'll call us a community, industry and the Agency together, because what we do generally is we say either there's something that we've determined during design can handle certain conditions and not handle other conditions. We put temperature controls in place. Then we put a cold supply chain in place if it's subject to below 40° F or that type of thing.

So the things that are very obvious to us, we know how to test for that and figure it out. What we don't really do is, in our risk analysis, we don't have those couple of key questions that say, and what if it goes outside of that extreme? What do you do?

So I think that our -- the questions we ask -- and it comes, I think, from the medical device directive, to be honest, around how you ask questions in your essential requirements, right, and doing your risk analysis, the questions that we ask around environment are in the manufacturing environment and they're in the use environment. There are really not a lot of questions around storage and distribution. And we use distributors. Let's

face it, we use suppliers, we use distributors. And so getting a better handle on either monitoring or controlling and knowing where our product is, that may be the opportunity that just isn't anywhere right now. It just doesn't exist in our quality regs, you know, the MDD and so forth.

So I'm just thinking off the top of my head that we could all ratchet down and use the QSR and get better at this. We all know how to do an investigation and say, hey, we had a fire. We had to go do X, Y, Z. It's expensive. You know, maybe more expensive than designing it in. We know how to design things in, under our own roof or under the user's roof. But this sort of in between, in the truck, on the shelf, right, is the packaging robust enough? Do we label to say what temperature conditions, what lighting conditions, and so forth? That may be where the opportunity lies.

MS. SCHUENEMEYER: Terry Schuenemeyer, the Public Representative.

When we were sent this packet of information and asked to read it and evaluate it for a decision as to whether or not the Quality System regulations were approvable or acceptable as they stand, the more I read them, and I read them several times in regard to this information about extreme weather, I found myself thinking that industry does do a good job. The Quality System regulations, probably the way they are written, do cover the manufacturing process. But all of the extreme weather conditions, as you were just alluding to, are outside of the manufacturing process.

And I think that, as was mentioned earlier by Ms. Kimberlin, the management control is where the ultimate responsibility would fall in the Quality System regulations. And to possibly think about making that part of the regulations more robust so that it's very clear that if your distributor or if your end product user suffers from an extreme weather event, perhaps the manufacturer would take the next step and go to look at the product and say did it -- not did it, was it affected? Was the temperature too high? The electricity was out for two weeks. It sat on the shelf in 100-degree weather.

And I think that it would be the responsibility of the management control as opposed to the current design controls. I think that your idea of possibly looking at the distributors is a good idea also. But we need to make the step to the end product user, the public. The product is already sitting on the shelf, it's already gone through all of its validation, and what do we do with it now? Can it be reused? Can it be reprocessed? Those are possible areas that we could discuss this afternoon.

DR. ZABRANSKY: Ms. Fiore, this fits right into where you fit now. Can you respond any further?

MS. FIORE: My concern is mainly oxygen. There are 1.8 million people in the United States who are dependent on oxygen. And it is a prescription medication, but it's dependent upon the durable medical equipment to be administered.

And the big problem that I don't -- is that in these emergency

situations, the first thing that goes out is electricity, and so much of the delivery systems are dependent upon electricity. I feel that the FDA should make some kind of requirement that there be a non-electrical backup system available to those patients who are oxygen dependent.

MS. BLACKWOOD: We do have that for, like, ventilators, right? So ventilators are required to have not just a battery backup but also a bag, right, that you can -- right. So I don't know much about oxygen. It's an interesting point.

MS. FIORE: Edna Fiore again.

There are portable oxygen concentrators which are battery operated. But in order to -- they have a very short duration, really less than a day or less than eight hours in general, but they require the electric backup. What I'm thinking about is the hard products such as tanks or liquid oxygen.

And we are running into problems with CMS because they are cutting down the -- under the competitive bidding, they are cutting down the reimbursement to about 25% of what it was a year ago or several years ago, and we're losing so many of the smaller providers because they just simply can't afford to stay in business. And this is going to affect so many people, particularly in rural areas and outlying areas. That is something that really needs to be addressed.

DR. ZABRANSKY: Well, the availability of the product that you're talking about, of air, is important, but the cost does not fit within the

FDA purview. Okay.

MS. FIORE: Well, I brought that up because there has been -- the product is no longer available because of this situation.

DR. ZABRANSKY: Ms. Olivera.

MS. OLIVERA: Mary Olivera.

Handling and storage of the medical devices, or any device, can really affect the integrity of that package. In my field of work, we have to read instructions for use in order for us to know how to handle that package, and a lot of times you don't get clear instructions or parameters on how to store those devices. And it would be really good if you got specific storage parameters, how high from or how low from the ceiling, what temperature and things like that, so we can have a clear understanding on how that package should be handled.

MS. BLACKWOOD: No, I think the international guidance on some of the symbols, like for expiration date, temperature controls, it's sitting right on the primary packaging, which I think is great. I agree, it should not be buried in the IFU because, let's face it, the IFU is sort of for reference, right? You're not going to -- it's not going to hit you in the face as your technician's loading up your inventory, right? So I understand that.

I'm just wondering what isn't there. So I do think that temperature and expiration and manufacturing date is typically on the primary packaging. What's not there?

MS. OLIVERA: In some packages, temperature is not clearly stated.

MS. BLACKWOOD: Okay.

DR. ZABRANSKY: Dave.

DR. CRANMER: This is Dave Cranmer. I wanted to follow up on Terry's comment earlier about the management subsystem.

In order for management to make good decisions, they need good data. And some of the kinds of things we're talking about, you don't have that during storage. So possibly being able to incorporate temperature sensors or RFID tags that tell you this is what happened in that packaging while it's in storage might be worth considering as a -- I'm thinking of it more as a guidance document rather than revision to regulation. But it goes to the notion of what are the better practices that are followed by manufacturers that know what they're doing.

MS. BLACKWOOD: We do use things like that in cold chain. So if we specify it's got to be at these conditions, especially the biologics, right, and some of the pharmaceuticals in particular, if they're active, in other words. So the technology exists to put a tag on it. It's big, right? So it's not a sticker like we do have with ETO. But that might be a good practice that we have in industry, that maybe we want to prescribe that in the user community so that they do know if I have temperature controls. It's all well and good that it was in there on the truck. But like once I drop it off, it's good

luck, right? So I think that's a good practice that we could share.

DR. ARMSTRONG: Brenda Armstrong.

Much of what we're talking about is reactive. It's what happens after the fact. And one of my concerns is that the huge amount of data that has been culled after the fact hasn't translated or may not be translating into modeling of products and chains prior to the introduction of the products or the release of the products for use in the general population.

And I'm wondering if there is the ability to require a more intensive modeling of the circumstances that we now have data from, before we actually then allow new products to come on line or as we provide guidance in terms of the specs around those products. And if that is the rightful -- or if it's not the correct purview of the FDA, whose purview is it to ensure that the information that we have now is translating back into better design and testing before release of product?

MS. BLACKWOOD: I was just going to comment on what, sort of, we currently do to substantiate the label claims associated with storage conditions and shelf life. Obviously stability testing for pharma. And for a lot of devices, now we do stability testing, meaning we leave it in a chamber under certain conditions and then we test it at some frequency during its life. And if we find a problem, then we go make a decision, otherwise. But generally we don't, if that was designed in that way.

So we have the design and the monitoring of the expected

operational conditions, which includes a little bit of a safety factor on either side. And that's based on what I'll call industry standard test methodologies. We do have accelerated aging because it's just faster, so we can go and ramp up the temperature or the pressure, that type of thing. We do have chambers.

But that's why I was asking Kimberly if there was a way that -- for industry to say FDA's anticipating that, for these kinds of classification of devices, you need to go and test not just for shelf life conditions on the label claim but also for extreme conditions because of the impact of those extreme conditions. Even though the likelihood is not high, the probability of harm is too extreme to take the risk, right?

So I don't think the manufacturers could possibly do that for everything, and I don't know if the juice is worth the squeeze, right? But on the critical devices, that might be the sweet spot that we pick on to see. And we would need a standard test method, you know. So that would be something we'd have to get with ANSI or AAMI on.

DR. KIMBERLIN: This is Cecelia Kimberlin, the other Industry Representative. I want to build on Dr. Armstrong's comment.

As I sit and listen to your comment, and Terry's and others', one of the takeaways I'm getting to is that are we thinking about this issue holistically enough? If you go back a decade or so in medical device design and development, we have a whole new translation today than we did then,

about use and use error and user error, and the Agency has been very formidable in helping us get new thinking. So now we have a whole body of guidance around human factors. So we thought more holistically about the use of our products.

So as we go forward, again, rather than being proscriptive on something that, as Liz pointed out, may not be really applicable to every situation, but is there some way of looking at this differently to say, when you do risk management of critical devices or devices that, if in short supply, would create a public health issue, do you include not just product use but a broader aspect of supply chain, how you interact with your customers differently? And that becomes part -- the best place for that to happen is during the design of the product.

So this broader guidance on this, targeted to specific critical use issues, I think, would be extremely helpful. And industry would be very willing to do that. Probably they do it in some extent today. But since there's no specific umbrella guidance around it, like there is, for example, with human factors -- if you look at human factors practice today versus a decade ago, we've all come a long way to the benefit of our patients.

MS. BLACKWOOD: Yeah. I think a great example -- and it gets back to the nylon. I don't know if you guys remember. I guess it was probably back in the late '80s when catheters were hot, right? They first started out and the industry didn't -- wanted to use this barium sulfate to put

in it so you could image it, right, so you could see the catheter. Not just the RO marker and where the tip and the balloon were, but you could see the whole catheter. So barium sulfate was something that we put into the extrusion compound with the nylon, and it would embrittle the nylon generally in high heat conditions, which didn't happen very often. But certainly when UV light bulbs became hot, it was an issue.

So industry got together, FDA, we talked, and you could not get anything approved without a foil pouch. Do you remember that? I don't know if you guys remember that, but you had to have -- and the hospitals went a little bit bananas. It's like, well, I want to be able to see my catheter through the pouch. I want to see what curve I have and so forth. So we had to do kind of a tradeoff, and that became a design packaging norm for storage for catheters, as an example, because so many were made out of nylon. And the docs wanted the barium sulfate, the nurses wanted to see the device through the package, so we put pictures on the outside, right? That helped. But that's an example where we had to do that because we were aware of a situation.

So I think that we do need to somehow target it. Whether it's by class of device or a certain type of device, we want to think about how much do we want to invest, as a society, in packaging, storage, chain of custody, because you can control everything and it just wouldn't -- I mean, healthcare is not getting cheaper, right, I mean just in terms of what we can

afford and the population aging and so forth. So I think we have to be really surgical about this and thoughtful about which devices do we want to go after if we want to put some guidance in around design and risk.

DR. CRANMER: This is Dave Cranmer again. I've got one more issue that I'm going to put on the table.

We've talked a lot about the manufacturing processes themselves and the devices themselves. A lot of extreme weather events become non-issues if the facilities themselves are built correctly with the right backup systems, with the right flood prevention techniques and tools. FDA, I know, has exactly no control over building codes, and I don't think they want to go there. But there may be a longer-term opportunity project for FDA to start to work with building owners and managers to figure out how to mitigate some of that nonsense.

DR. ZABRANSKY: Yeah, I guess we have to build a dike around every warehouse, right?

(Laughter.)

DR. McNAMEE: This is Scott McNamee.

One of the areas of discussion that I hope the Committee will consider this afternoon is much of what you were saying before, in terms of identifying what are the areas around which we need to define the new normal. Whether that new normal is in the area of storage and transport, manufacturing, use environments, where do we get the best juice for the

squeeze? I love that expression. I'm going to steal that, thank you. Because there is always a cost associated with when you change things, but there may also be -- it may be very much worth the cost. But that's for the Committee to discuss.

Are environmental conditions within the home so variable, in light of the rate of extreme weather events happening, that there ought to be a push to educate users? Are there particular types of devices that this consideration is more relevant to? Is the question of the durability of a device and the way it's used more appropriate for a particular subset of medical devices or another? Those kind of discussions, I hope, are part of what will be going on this afternoon.

MS. BLACKWOOD: This is Liz Blackwood again.

We should probably think about where in the home-use guidance, because I know that's kind of on the cusp here, right, because you've got glucose strips, right, and Mary's going out for the afternoon and she's going to put three in her purse. Bad idea, Mary. She doesn't know that, right? You've got this desiccant, right, that they come in. So I think the home use, it's a whole new frontier, and there will be more home use as we have less availability of beds, right, so home care. So I think that's a good point, and I think maybe we want to hit the home use guidance with whatever the thinking is.

DR. ZABRANSKY: Okay, at this time we're going to proceed on

to the Open Public Hearing portion of this meeting. Public attendees are given the opportunity at this time to address us, the Committee, to present any data, information, or views relevant to what we've been talking about.

Ms. Facey again, here, will read the Open Public Hearing disclosure process statement.

Natasha.

MS. FACEY: Both the Food and Drug Administration and the public believe in a transparent process for information gathering and decision-making. To ensure such transparency at the Open Public Hearing session of the Advisory Committee meeting, FDA believes that it is important to understand the context of an individual's presentation. For this reason, FDA encourages you, the Open Public Hearing speaker, at the beginning of your written or oral statement, to advise the Committee of any financial relationship that you may have with any company or group that may be affected by the topic of this meeting. For example, this financial information may include a company's or a group's payment of your travel, lodging, or other expenses in connection with your attendance at the meeting. Likewise, FDA encourages you, at the beginning of your statement, to advise the Committee if you do not have any such financial relationships. If you choose not to address this issue of financial relationships at the beginning of your statement, it will not preclude you from speaking.

DR. ZABRANSKY: Thank you.

Now, at this point, does anybody wish to address the Committee at this time? If so, please do come forward, state your name, affiliation, and indicate your financial interest, as Natasha just went through. Each speaker will be given five minutes for their presentation.

MR. TYMINSKI: Good morning, sir. My name is Will Tyminski, and I am an independent emergency manager. As far as my affiliations, let's just say I'm a free agent.

And as you're going into your deliberations this afternoon, and having listened to the session earlier this morning, I would recommend to the Committee that you do so in light of the national response framework, because that is the methodology of which the United States approaches large-scale weather events or any other kind of adverse effect event that affects large populations of persons.

And by doing that, specifically the emergency support function, which deals with public health, you'll find out where your efforts integrate and synchronize with the greater plan. And then you'll also find that there are certain things that you will do in preparation, certain things that you're going to do in response to an actual event, and then some certain things that you're finally going to do when you transition to a regular state of operations.

Thank you.

DR. ZABRANSKY: Thank you, sir. Again, your name.

MR. TYMINSKI: Will Tyminski.

DR. ZABRANSKY: Thank you.

Any other individuals wish to address us? Here we go.

MS. ABDUL-MAJID: Good afternoon. Mujadala Abdul-Majid. I am with 3E Company. They will probably pay for my coffee today. We're just down the street in Bethesda.

I'm sitting here and listening. I didn't have a formal presentation prepared, but I'm hearing a lot of comments that sort of speak to what we do. I'm not in sales. I'm a regulatory analyst with the company. But I wanted to just put out there, that the data is out there.

When it comes to FDA's role in critical supply chain for medical devices, it's very downstream. We're talking about finished products. There are very robust areas that go into the supply chain. I think, as you mentioned, FDA can't regulate the cost. FDA can't regulate a number of things that go into supply chain concerns.

And what I've been doing a lot of lately is talking to various sized companies in the drug and device sector, and the larger companies have people in charge of supply chain, people in regulatory, and when it works well, they work together to see where the overlap is and what part of compliance falls into their bottom line and how they manage that. It really falls to component parts, where they come from.

Everyone's forecasting is sort of three to five years out. It's not just weather conditions that can affect that. You have Dodd-Frank affecting

companies' supply chain with conflict mineral speculations, and that being a part. That's going to be implemented in less than three to five years out, and companies are struggling to figure out how that affects their finished product. And when you're talking about the better companies that will use three suppliers rather than one, whereas those three suppliers source by the same one subcontractor, it really is a global issue.

I think, when you're talking about FDA's role and what they can do, QSRs are flexible. They're as flexible as they need to be. They are as broad of scope as they need to be. I think the best thing is, too, if you issue a guidance document, industry response to guidance documents and reminding -- and that guidance document should remind industry that they are responsible for their supply chain. And I think that's just -- the best route you can go is a strong reminder of that, and a reminder that these data solution tools are available and they should be using them. I mean, the data is there. It's just a matter of reaching out, and that's what we're doing, basically.

DR. ZABRANSKY: Thank you.

Any other public speakers, please?

(No response.)

DR. ZABRANSKY: At this time I'd like to ask the Committee if they wish to ask any questions of the last two presenters.

Yes.

MS. RICHARDSON: Hello, I'm Susanne Richardson from the New England District Office, and I conduct some medical device inspections. And I have an easy solution -- or not a solution, but a suggestion, is that if CDRH is monitoring, keeping track of any extreme weather conditions that could affect our medical devices around the world, that they could include this in the individual assignments that are being sent out to the field. If we know, if that information comes to me in the field, then I'll be able to check and follow through on any concerns that might be from suppliers or any others.

Thank you.

DR. ZABRANSKY: Okay, again, I'll ask the Committee if they have any specific questions to some of the folks that have just spoken.

DR. KIMBERLIN: This is Cecilia Kimberlin. Not a specific question, but perhaps a comment. And maybe the Agency folks can help clarify this.

You know, I think it's one thing to think about the activities that a very large firm, a large medical device company, can do. But it's my understanding, if I remember the data, that a large portion, a large percent of medical device manufacturers are actually small firms. Maybe you can help us understand it because again, to the credit of the flexibility and the approach here, and using risk management and all of those other things we've talked about, I think we have to be very thoughtful about making

recommendations that can truly be addressed on the broad spectrum by medical device manufacturers. And some very critical and important devices are made by some very small companies.

So perhaps, Jan, you could help clarify.

MS. WELCH: Right. Not that I sort of have instant data right off the top of my head, but just I know, over the last few years, like 50% or 60% of the device manufacturers are 10 employees or less. I mean, it's really a very small business orientation, as you said.

But I was thinking to what Liz was saying. We used to have this term, critical devices. We had a critical device, we had it in the '70s and we had it in the '80s. We don't do that anymore. So I was listening to what you were saying and was listening to what Kim was saying about Class III devices, obviously the highest risk. But maybe where we get into some of this is how to tease that out. And is it by panel? Is it sort of by the sector? And then you're looking at what are those most critical devices or most critical technologies or critical parameters, and we prioritize it that way.

So it doesn't matter whether you're a five-person company making it. It is still the same as if you are the huge firms making it. That is that vital product, it's that vital technology, and everybody has to take those things into account. And how we tackle that and how we prioritize that, we need to work on that.

DR. ZABRANSKY: Are there any other -- pardon me? Oh, I'm

sorry, go ahead.

MS. SCHUENEMEYER: I'd just like to ask the second woman who came up and spoke, what company are you from?

MS. ABDUL-MAJID: 3E Company.

MS. SCHUENEMEYER: And what does your company do?

MS. ABDUL-MAJID: We do supply chain data solutions. And it's more than regulatory. I mean, it's really compliance. So that's a broad spectrum when it comes to -- from a global perspective, there could be transportation compliance issues, trade negotiations that firms should be thinking about that may affect their supply chains. So really it is like you said before, a holistic approach to compliance. And I'm not here from sales. We're not the only company in the game. I just think that firms should be thinking about the fact that these solutions are out there and utilizing them.

MS. SCHUENEMEYER: Thank you. The reason I wanted to clarify that is it brings to mind that FEMA works closely with hospitals whenever -- a lot of these tragedies are predictable. You know at least a week in advance, sometimes more, if a hurricane is coming in your direction. Some of them aren't, like the Arizona dust storm. But in the cases of the ones where you know that something is approaching, you can start working early on to mitigate whatever your problems are going to be downstream.

And I was wondering if larger -- I expect larger companies do have processes in place for this, and I wonder if they know if any of the

smaller companies do have processes in place for this, also, or the 10 employees just evacuate. And if anybody has any information about that, I'd be interested in hearing it.

MS. BLACKWOOD: Are you talking about evacuating the manufacturing and distribution office facilities? Is that what you mean?

MS. SCHUENEMEYER: No, I'm talking about, for example, at our hospital. If there is a chance that something -- if something develops in the Gulf, we're in Houston, Texas, so we often have development in the Gulf of Mexico. If something develops in the Gulf and it is five days out, then our research institute and hospital, on a certain level of preparedness, we start to check the backup emergency generators. You know, they check what is in stock, what of our critical products do we have on the shelf, and start getting them in. And then they also have stocking areas 100 miles out or 200 miles out, where you can bring facilities that you may need in and put them to where they would be available if you need them later.

As the hurricane gets closer and closer, the level is increased and the different departments have certain things that they check. For example, if the roof blows off, then, are all of -- or the windows blow in. At 48 hours ahead of time, everything that's critical in paperwork, all of our data is moved to an area that wouldn't be affected by the water coming in from the window. We can't help it if the roof comes off, but we have backup systems where everything that is critical is scanned and on more than one

server, and servers that are in different locations, not just servers within our building.

So I'm wondering, I would expect that a large industry, like Abbott, would have processes in place like this where, as the problem is approaching, you're working step by step on the solution. But with the smaller companies, the 50% to 60%, is there anything that tells them -- is there anybody who tells them to put these kind of processes in place? Or, you know, do they just shut down their processes and evacuate?

DR. ZABRANSKY: I can comment on that. I'm a member of our local emergency planning committee for a county, and the only jurisdiction or the discussions we have with companies are those that have materials stored, let's say, ammonia or products like that, that could be released in the case of such a natural critical event. Any small companies in the area, unless they want to -- this is a tall event. The role is upon them to initiate the discussions with the emergency planning committee. And, again, a lot of this is all supported through FEMA directly from the Fed down to states and then spread out to regions and into the local counties.

MS. SCHUENEMEYER: I guess maybe something else we would want to consider in our discussions this afternoon is what kind of guidance to give industry on planning for these events to happen.

DR. CRANMER: FEMA is the lead agency for that. This is Dave Cranmer. And if you go to their website, they, in fact, have a voluntary

program for businesses for emergency preparedness. All of the training and guidance you could possibly want is there.

But as a small business owner, I'm not necessarily going to follow it, and it sort of depends on my, as the owner-manager, analysis of the risks and the rewards, what of that I do, what of that I don't do. The smaller I get, the more likely it is. It's like a tornado is coming. I'm going to get in the storm cellar, because that's the time frame I've got. Yeah, if I've got a hurricane, I can move. If I've got a tornado, an earthquake, or something that's a little more sudden than that, it's not necessarily an option. And I may or may not have made my facility that event-proof.

DR. ZABRANSKY: Okay, thank you.

At this time we will -- we're going to break for lunch. This concludes the Open Public Hearing portion this morning, and we'll break for lunch. We are about a half hour early; however, we've notified the hotel ahead of time that we would be a little early. The Committee itself is going to be in a separate area of the dining facility. Someone referred to it as a fish bowl. If you were in there this morning, you saw it had a big glass front on it. There's a separate room that's reserved for the Committee. We will resume promptly at one o'clock, so please be prepared.

Committee members, please do not discuss, even at the table in there, anything that we've talked about this morning amongst yourselves. Everything has to be recorded, what we do and what we say.

Okay, let's see if there is anything else here I'm supposed to look at. We're going to resume promptly at one o'clock.

All right, thank you very, very much.

(Whereupon, a lunch recess was taken.)

A F T E R N O O N S E S S I O N

(1:00 p.m.)

DR. ZABRANSKY: All right, good afternoon. I'd like to resume the Committee meeting.

We're now going to proceed with the second Open Public Hearing portion of this meeting. At this time members of industry, professional organizations, and societies will be given an opportunity to address the Committee, to present data, information, and their views relevant to our agenda.

Again, Ms. Facey will read the Open Public Hearing announcement disclosure.

MS. FACEY: Both the Food and Drug Administration and the public believe in a transparent process for information gathering and decision-making. To ensure such transparency at the Open Public Hearing session of the Advisory Committee meeting, FDA believes that it is important to understand the context of an individual's presentation.

For this reason, FDA encourages you, the Open Public Hearing speaker, at the beginning of your written or oral statement, to advise the Committee of any financial relationship that you may have with any company or group that may be affected by this meeting topic. For example, this financial information may include a company's or a group's payment of your travel, lodging, or other expenses in connection with your attendance at the

meeting. Likewise, FDA encourages you, at the beginning of your statement, to advise the Committee if you do not have any such financial relationships. If you choose not to address this issue of financial relationships at the beginning of your statement, it will not preclude you from speaking.

DR. ZABRANSKY: Again, if anybody has any cell phones, make sure you please silence them at this time.

Now, does anybody wish to address the Committee at this time? If so, please come to the podium, state your name, affiliation, and indicate your financial interests, as Ms. Facey has just described. You'll be given five minutes or so.

(No response.)

DR. ZABRANSKY: Apparently we have no people that want to address us, so at this time I pronounce that the industry, professional society, and organizations Open Public Hearing oral presentation session will be officially closed. We will not take any more speakers at this point.

If there's any of the -- oh, let's proceed on here. Before we proceed for the rest of the agenda, the Committee will now hear a presentation from Dr. Philip Ferro from the U.S. Department of Health and Human Services, who is Assistant Secretary of Preparedness and Response.

Dr. Ferro, you may begin your presentation now. Welcome.

DR. FERRO: So thank you, everybody, for having us today. We're very excited. Dr. Lurie sends her regrets. She had to stay downtown,

so I'm presenting on behalf of our group today, and we'll be talking to the Advisory Committee on building health resiliency technologies.

With that, I wanted to move into a little bit of background for folks who aren't familiar with ASPR and what we do, and even the concept of health resiliency technology. Because we coined the term, so we should probably explain it. But really the purpose of this presentation is to present an example of how the government is working together in an interagency fashion to enhance public health. It's really, we think, a very good news story. There's a really terrific collaboration between FEMA, ASPR, and FDA and that's going to get to a lot of what's going on in this presentation.

As far as ASPR, for those of you who aren't familiar, the Assistant Secretary for Preparedness and Response is responsible for leading the nation in the prevention, preparation for, and response to adverse health effects from public health emergencies and disasters. And this is a very broad mandate. It ranges from everything such as pandemic influenza, to weapons of destruction, to the derecho, to Sandy. So we are responsible for a very wide variety of hazards, and we really have started to think about this from an all-hazards approach because of the breadth of what we have to do. Especially when you keep in mind the vast geography of the United States, the permutations that we have prepared for are immense.

Regarding health resiliency technologies, what we envision these to be -- and this is an evolving process because this is a new initiative --

are technologies that allow individuals to continue to use their durable medical equipment or devices that are powered by electricity during disasters and prolonged power outages, and this in order to enhance community resiliency as well as individual resiliency and public health.

Examples of this would be sensor signaling devices that interact with durable medical equipment, universal batteries that can be utilized by all DME, and batteries or power generation sources that don't rely on electricity and can be used indoors for prolonged periods of time. So we're not talking about taking a gas generator and hooking it up. This is something you can use in an apartment in the Rockaways on the 30th floor.

A little bit about the team. This is an initiative the Secretary selected. There's a new program called HHS Entrepreneurs. The Secretary, Secretary Sebelius, selected four initiatives that are meant to address some of the toughest challenges the department is facing and to build teams of internal and external entrepreneurs. And these are folks who have demonstrated ability in and outside of government to be change agents and to take on tough problems and develop innovative approaches to solving them.

So our project was luckily selected as one of the four. Our external entrepreneur is Mr. Frank Sanborn. So Frank comes to us by way of a nonprofit he started, but then before that, Microsoft. So he has a very strong technical background, and he has a very deep interest in devices and

disasters, and that's what his nonprofit is focused on. So he's been a terrific asset.

Our internal team consists of Dr. Lurie, who is the Assistant Secretary for Preparedness and Response; myself, the Director of Special Projects; Stacy Elmer, who is the -- she's a special advisor to Dr. Lurie as well as the CTO of HHS; Mr. Ted Okada, he's CTO of FEMA; and Desiree Anderson, who is the Chief Innovation Advisor to the Deputy Administrator of FEMA.

Again, given the complementary mission space that both of our groups occupy, we thought it was really, really important not to build silos but to really work to break them down and to develop any synergies we could, in terms of how we go about doing our mission so that we can do them Rockaways better.

And with that, I will jump right into how this project got started. And it really got started with an observation. As everybody in this room knows better than most, there are many folks in this nation who are dependent upon durable medical equipment. Whether it's a ventricular assist device to help them pump blood, or it's an oxygen concentrator to help them breathe, these devices are central to their health and well-being.

However, during a disaster or a power outage, such as Sandy or the derecho, we are faced -- they're faced with a particularly nasty problem, and that's twofold. One is that all of sudden there's no electricity, and the other is quite often the communications infrastructure is down or destroyed.

And you don't know what the damage is going to look like ahead of time, and that is a very difficult situation to be in, because all of a sudden now, as soon as your batteries run out or the power goes out, you've got to find a way to charge it. And I know this group is acutely familiar with that situation.

The challenge becomes that they have no way to communicate their needs to friends, loved ones, emergency response, and what often happens, if they're lucky enough to be ambulatory, they're going to head out into a disaster-stricken area, which is not a good thing, looking for power. They may end up in a medical shelter. The shelter quite often doesn't have the ability to deal with special needs requirements of medical devices, so they quite often end up in the ER. So now you've got a situation where the ER that's already trying to cope with all of the elements of the disaster that they're trying to deal with from a medical perspective has the increased burden of folks that probably could've sheltered in place or linked up with folks in the community to get them what they need.

For the folks that aren't ambulatory, the situation becomes even more dire. There now, since they can't communicate and they can't get out in the public and we don't know where they are, we don't have a good way of locating them and providing the assistance they need. We end up knocking door to door, asking neighbors, asking friends. So critical time is passing before these folks get the assistance they need, if they get it, in a timely fashion. And that's really the -- that observation was the basis of this

project and why we wanted to do this, because we thought there's enough technology out there, and there's enough folks that are looking at this problem, that we could find a solution to it and mitigate a lot of the public health burden as well as building up stronger communities and enhancing our ability to respond to disasters.

So as I kind of touched on in the last slide, and I think the group is probably -- you guys are, I'm sure, aware that it's not a point failure that led to this observation. It's really a systems failure that was contributing to this. And there are three broad categories of what we've identified as the failures and how we're going to address them.

The first is in populations and location. So during a disaster, or right before, if it's something we know is coming, if it's not an earthquake, if it's a storm that we know is coming, like a hurricane, we don't know what populations, what individuals within the communities utilize these devices. We don't know the location. And that's not only static information, but it's active, dynamic information because folks are moving around during a disaster. And, lastly, we don't know what's the status of the device. So we don't know where they are, we don't know who they are, and we don't know are their devices working? Do they need help imminently, or do they have some time?

The next is related to power. There are currently no good universal batteries capable of powering these devices. There are no

alternative powers. Again, you can have a gas generator, but not ideal. And shelters currently are not well equipped to handle these individuals. And there are anecdotal stories that you would hear of a couple people who had to hook up their devices, and they blow out the power generation at the shelter, and now you've got a whole other problem.

And the last category is communications, and that's tools and infrastructure.

And those really are the three categories that we're seeking to address with our integrated parallel approach. And for those folks or people who are on the phone or on WebEx, I'm on Slide 5. But that's really how we've begun to structure how we are addressing this problem.

And so from a population, location, and identification standpoint, we really have two major efforts going. The first is developing a prototype device, in house, that is capable of interacting with durable medical equipment, and it can sense -- it will be able to sense, or it can -- we have the prototype, we built it. It can sense when the power goes out, what's the status of the battery, what's the health of the battery, what is the location of that device, and it can put a time stamp on it.

Commensurate with the all-hazards preparedness posture we're trying to adopt, you can imagine, if the power goes out at cell phone towers, you've got no power for -- you've got no CDMA or cell phone service. If the power goes out, generally you're not going to have Internet. So this

device is also capable of transmitting over multiple spectra so that no matter what bandwidth is available, we can communicate over that. And we're also working with the amateur radio community, which is very active in disasters, to be able to transmit over amateur radios. So again getting to that ability that you can get the information out and get those people help in a timely fashion.

Understanding that industry adoption is going to be absolutely critical for this work, we're also working with FDA, which is why we're here, and we have a wonderful partnership with CDRH, to begin to identify and start to think through what are some of the regulatory and policy issues that we may need to address.

Additionally, we're working with BARDA, which sits within the ASPR, and that's the Biomedical Advanced Research and Development Authority. We're working with them to begin to engage industry and also think about what a procurement might look like down the road. There are no plans for that at this time, but, again, we're trying to plan as far ahead as we can.

Separate from that, but related, is we're working with CMS to use claims data to begin to identify, based on claims data, populations or areas within communities that may have a higher concentration of folks that depend on devices. And the rationale behind this is, if we know, for example, in New Orleans that particular neighborhoods have more CMS claims data for

devices, one could postulate that there is probably a higher concentration of folks who live in those areas that are going to be dependent upon devices during a disaster. And you can use this in a couple of ways. One would be if you could work with power company to say, okay, we want to prioritize power restoration in this area, or for our emergency response or disaster coordination centers to be able to say, look, you're going to really want to focus here. You're going to have more population that's particularly -- that may be dependent upon devices here.

So really it's knowing where your folks are and knowing what their status -- you know, the status of their durable medical equipment is. And this is all going to be piloted, both of these threads of work are going to be piloted later on this summer in New Orleans. In June, actually, at the start of hurricane season. So we're working very diligently to get everything together.

Given that this is a device group, I wanted to touch on more of the sensor prototype, because I think that'll be of particular interest to this group. And it also shows just how far and readily available the technology is.

We've adopted two overarching concepts for this project. One was to be open source and the other was to engage the community. So all of the IP that's generated from this we have patented and put in the public domain with a limited use license. The prototype device that we've built, we actually -- it's completely open source and we bought off of Maker SHED on

the Internet. Maker SHED up on the Internet. And we were able to build this prototype with basically things that are readily available online, completely commoditized, completely scalable, and readily available. I think our prototype sensor is about $130. That's retail. So it just shows what the technology can do and how commoditized and low cost it is, and with a little bit of knowledge, what you can do with the technology.

From a software perspective, again, we're using all open source software as well, and this is because we really want to engage the community. And that moves us to Slide 7, getting back to the community engagement bit.

So utilizing an open IP, utilizing open source hardware, utilizing open source software, we've been able to get a lot of interest and a lot of engagement from the maker and coding communities, and they're very excited about this because there is a huge -- for folks that aren't familiar with the maker communities, there is a huge, huge grassroots group across the nation, across the world, that are really working to build things, and it's a really exciting time because they're using electronics much like the Homebrew Club in Silicon Valley back in the '60s and '70s.

These guys are really -- it's a very vibrant community, and they're very excited because now they have something to catalyze them to come together and work for the common good. So the non-industry, the community aspect, has been wonderful and we want to keep it that way. So

we are working with a lot of folks, keeping everything open source.

The next thing is, we see ourselves really as a first mover here. We don't have the final solution. We're a very small group. We want this to really go out into the community and be built and be adopted by industry. And so what we're doing as well is we're getting ready, probably in the next month or so, to post a maker blog, and this is that anybody can log on and they'll have basically a recipe to make their own sensor signaling device. And that really gets things back out to the communities. We'll post all the code, we'll post the bill of goods that are needed and put all the instructions online. And, again, it's really getting back to the community involvement.

So moving on from where folks are and who they are, to infrastructure and tools for communication, the next thread of work really relates to communications infrastructure. And I've touched on this already. I'm sure many of the group here are familiar with MBAN, or mobile body area networks, familiar with Wi-Fi, cellular, amateur radio, and mesh networks. These are all communications infrastructure that we want to have able to not only interact with our device but be able to deploy during a disaster. What we saw in Sandy was the ability to set up mesh networks for Internet access was critical, not only for getting FEMA to be able to process claims more quickly, but for getting that community resiliency aspect to really come together very quickly because, from a mental health perspective, when folks are connected, they're stronger. And so we're working not only to develop

the infrastructure that's necessary, but we want to make sure our devices work with a number of different types of infrastructure.

The next logical question becomes okay, great, you guys. You have a sensor device. It's signaling. Where's it going? We are working on developing -- we are currently developing a platform that will serve as a data mark that is a data repository to take all different types of data coming in and put it together in a way that -- in a secure fashion that can get the right folks the right information at the right time. So it's a place for this data to go so that emergency response, community activation groups, authorized folks will be able to have access to this data; again, getting back to the resiliency component.

From a communication tool standpoint, we see competitions, challenges, and code-a-thons and make-a-thons to support community innovation. That is in part to help us get a better mousetrap. But the other aspect is to really broaden awareness of this. We really want this to be a grassroots effort as much as it is being driven on the industry adoption aspect as well.

And, lastly, from a communication tool standpoint, we see this -- you know, things that are used on a day-to-day basis are going to be used during the disaster. We think there's a broad applicability to this technology during day-to-day, whether it's helping grandmom and the son or the daughter to stay in contact during the day so they don't have to check in

because they know their medical device is functioning properly, or if it's just to help people to communicate with one another better and feel a sense kinship and camaraderie. We think that social media is going to play a big part in this, so we also are planning on launching some challenges related to social media applications for individuals and communities.

Moving to the next slide, that really encompasses the scope of what we're trying to do, because this is a one-year project. So we're actually going to be time up in about November. So we don't have a lot of time, so our scope is limited. But we realize the other components of this really relate to resiliency and power, which we've touched on.

Response infrastructure. And FEMA has got a critical role here in terms of revamping response infrastructure. There's a ton of work they're doing just outside of the scope of this talk.

Another is device and information security and privacy. As we begin to have more and more things with IP addresses, and as MBAN comes on line and devices start to integrate, we need to be acutely aware of the security challenges that are going to be faced, not just in terms of HIPAA and data, but of the devices. You know, there's evidence of folks who can hack into an insulin pump and get it to dump all of its insulin remotely. That's an example of the type of security we're thinking of here, not just data, but device security. And that's something that's at the forefront of what we're developing with this initiative as well. Our goal is to build the most secure

device we can, but then also to start to foster that thinking and that posture across the community. We would see that as a huge win in addition to this.

Power is the next very large component of this. We're working with the Department of Energy as well as the power industry to develop components of response frameworks and standard operating procedures, as well as ways we can use the information coming out of these devices and the networks we're building to either act as these early warning systems.

You can imagine, if you see devices start lighting up and sending out signals, that would probably indicate there's a power outage. And right now, currently, the best way that power companies know there's an outage, from my understanding, which is limited, is folks calling into the power company. So if we can have a way of automatically doing that, you could then imagine that power companies can respond quickly and get the power up and running.

And as I mentioned previously, power restoration prioritization. Is it more important for a community with multiple senior homes and high concentrations of device-dependent individuals to be prioritized over a regular normal neighborhood that doesn't have that? You can imagine where, from a public health and resiliency aspect, there could be great benefit to having that type of prioritization framework in place. So we're working with those groups as well.

And then lastly and most importantly, I think, are energy

solutions for patients and communities, and not only universal batteries, but the ability to again generate power. And to this end, we have an RFI out for anybody who's interested. There's an RFI out through BARDA, currently. It's a request for information, and it's threefold and it's focused, and it touches on this talk. It's universal batteries, power generation, and sensor signaling devices. Again, we see ourselves just as the first mover here. We do not see ourselves as the ultimate solution, and with the goal being a fully integrated system.

So, again, having a sensor signaling capability that we can generate actionable information for friends, family, and emergency management, community organizations, and then really inspiring industry innovation, and then also working on that power for devices aspect, in order to build an ecosystem to meet the needs of individuals, and again with the thought of whole community and industry support.

And with that, I can take any questions or anything that anybody would like to have addressed.

DR. ZABRANSKY: Thank you, Dr. Ferro.

Questions? A number of issues were raised this morning concerning relationships to FEMA. Now, you heard some of it.

DR. FERRO: Yeah, we work very, very closely with Administrator Fugate and Deputy Administrator Serino, and they've been wonderful partners in all of this.

MS. FIORE: Edna Fiore here.

Boy, you've blown me away.

DR. FERRO: In a good way, I hope.

MS. FIORE: I would like to find out whether I could have a set of your slides to provide for various support groups and so on.

DR. FERRO: Absolutely, absolutely.

MS. FIORE: Okay.

DR. FERRO: Yeah, these are public domain. You're welcome to them, and I'd be happy to provide them for you.

MS. FACEY: And this is Natasha Facey, Designated Federal Officer.

All PowerPoint slides will be posted to FDA's website within 24 hours of this meeting.

DR. KIMBERLIN: Thank you so much for this very interesting and stimulating presentation.

Are you at a point yet -- I know you're in the early stages where you would understand what kind of cost impact this would put on some of these devices. As you know, some of them have been around a long time and they're under cost pressures. And then the aspects of redesign. And so, again, it depends.

DR. FERRO: Yeah, and that's a wonderful question. Our thought, again very early stage, is that we want this to be universal and not

actually -- ultimately, yes. You know, if we had our -- our vision is that in 5, 10 years from now, this type of technology will be integrated. This use case will be understood and integrated. How we're looking at this right now is that it could be a small add-on component that doesn't affect the performance of the device. That way it doesn't need FDA clearance and it's just an add-on and an added benefit or capability.

MS. BLACKWOOD: Not really a manufacturer's perspective here. This is Liz Blackwood, Industry Representative. But as an engineer, I was curious if you might consider, or maybe you have considered -- I spent a little bit of time in Africa, and they have power issues, as you probably know.

DR. FERRO: I worked in West Africa for a number of years.

MS. BLACKWOOD: Okay. So they have some really clever ways and means of getting power quickly, because it happens all the time.

DR. FERRO: Yeah.

MS. BLACKWOOD: Right? So I'm just wondering if there's some coalition there that you could tap into.

DR. FERRO: Yes, and we are. We're working with a number of -- we're taking a whole government approach. Actually we have a White House working group that is focused on disaster technology, and so we're trying to find out what everybody is utilizing and find out what the best solution for the use case is going to be and what that's going to look like. But absolutely.

MS. BLACKWOOD: Yeah, that's smart. I think just to forge the point here about the universal, that would make the adoption really fast, right, because I think we can all -- as manufacturers, society, healthcare, government, we can all see the case. But to have to revise your design, especially when you're talking about the software, yeah, I don't like touching the software unless I have to, right?

DR. FERRO: Absolutely. And it was interesting because, initially, when we were preparing the RFI, somebody said, oh, that's easy. You know, from the universal power and batteries perspective, we said, well, we don't think so. You know, there's going to be a fair amount of clever work that's going to need to be done to make this truly universal, especially when you think of just the broad range of power needs and device interfaces and everything like that. And I'm not a device expert, but that was our -- our supposition was, this is going to be a little bit more difficult than people think, and it's one of those bigger, bigger goals we're trying to address with this.

MS. BLACKWOOD: And Liz Blackwood one more time.

There's also another group working on wireless with FAA, right, FDA and FAA and industry working together on how to handle the interfaces and the universal interfaces between medical devices and systems. So I don't know if there's something that worked that they've done that you could leverage as well.

Jan, do you know what I'm talking about?

DR. FERRO: Is this the group where -- I think their annual meeting is coming in Portland pretty soon.

MS. BLACKWOOD: Okay.

DR. FERRO: Their name escapes me --

MS. BLACKWOOD: I'll think of it.

DR. FERRO: -- unfortunately, as well. We've reached out to them, and we're starting to forge a relationship with them.

MS. BLACKWOOD: Yeah, because they may have already done some of the wireless communications work, relative to universal interfaces, on infrastructure and --

DR. FERRO: Yeah. And so that's also what we're hoping to get from the RFI.

MS. BLACKWOOD: Yeah.

DR. FERRO: Again, we don't know what we don't know at this point.

MS. BLACKWOOD: Right.

DR. FERRO: And so we're hoping that -- and we're trying to reach out to as broad a group as possible, which is why we're delighted to speak here today. I think we're talking about the same group, and we have reached out to them and are talking with them.

MS. BLACKWOOD: I'll get the name of it for you later.

DR. FERRO: That would be wonderful, because anything that anybody has already done, even better.

DR. ARMSTRONG: Brenda Armstrong.

I would put the subgroup of children who are not in the hospital for a long time but for whom we move a tremendous amount of technology to their homes. And it dawned on me that -- and maybe I'm being a real idealist, but the potential to affect building codes down the road so that new buildings, homes, are put in a place where it doesn't take an act of Congress to move children and adults who need chronic support at home, because all of the things that you've talked about are part of the way that we build houses and the way that we put buildings together going down the road. The actual costs for us to be able to send a baby home who needs a feeding pump and oxygen and all of those things is enormous.

DR. FERRO: Absolutely.

DR. ARMSTRONG: It really is enormous. But part of it is being able to provide the electrical substructure that won't blow out everything in the house. The other piece of it is to give the parents or the families easy access without having to wait on a slow connection on the Internet. So I'm wondering if there's any thought about that going forward, and also to look at retrofitting existing homes in a way to allow that because, truth be told, our population is aging and at the same time our technology has allowed us to support very complicated issues for very complex children that ordinarily

would not have survived.

So it seems to me that working within the framework of talking to people who put houses together or put buildings together so that there is universal support should be on the agenda as well.

DR. FERRO: It's a wonderful point, and it makes me so happy. Everything you've just articulated is central through our premise that as technology increases, as our population ages, there's going to be more and more folks that are going to have increasingly complex medical conditions that are now going to be able to go back to their homes and to live their lives outside of a medical center. But we do realize it's going to impose a whole host of new challenges that, as government and industry and communities, we're going to have to begin to adapt to in order to make these solutions work.

And I think the part regarding building codes is brilliant. However, that's outside of the scope of what we do. And I'm merely HHS, but I would agree. And I think if this group is able to influence -- and it's certainly something I will bring up at the next disaster technology meeting that we have at the White House, to begin to discuss where we could go in terms of influencing building codes. But I think it's a wonderful concept, I would argue, just a little bit outside of my lane, so I don't want to -- I would not want to step on the toes of my other federal colleagues. But I absolutely agree with you.

MS. FIORE: Edna Fiore.

I would like to see this integrated with telemedicine systems.

DR. FERRO: I think it's a wonderful point, and I think that's ultimately if you think about where the technology is going. And this is getting to more of a telemetry aspect, almost. You can imagine, especially -- and that's why we specifically put in here MBAN, because our thought is that you could imagine, down the road, four or five generations of these types of devices from now, you know, when MBAN really is being adopted and it's being used.

This is yet just another component in that MBAN network hub, and it's another component of what that health status looks like for an individual. It's how is their device functioning? And if you see a spike, you can then look at -- you know, you begin to correlate the health of the individual with the device status and integrate that. But absolutely. And that's why we wanted to make sure that we put the MBAN component capability in there as well, and the compatibility.

MS. SCHUENEMEYER: Terry Schuenemeyer, the Public Representative.

This sounds great. I really think this is a wonderful idea.

DR. FERRO: Thank you.

MS. SCHUENEMEYER: And being able to improve the building codes so that the houses can more easily adapt to this kind of a situation is a

good idea. But ultimately, if a disaster is something that you know is coming, you would want to evacuate these people early.

DR. FERRO: Yeah.

MS. SCHUENEMEYER: And evacuate them to a facility that also has the type of backup powers, not generators, not battery power, but some sort of energy source. And I assume you're working also on that type of infrastructure.

DR. FERRO: FEMA is working diligently on revamping a lot of their response structure to begin to think about this as well, but I don't want to speak for them or put any words in their mouth, but they are thinking about that. And, ideally, our ultimate solution is that we have a system in place where these individuals can just shelter in place, or they've got enough community support that if their house or their home is damaged or destroyed, they can go to a neighbor and the neighbor will be able to care for them and really build up this community resiliency aspect. And then additionally, yes, the shelters as well.

But our real goal is to allow these individuals to remain in their home or have their community assist them and have real whole community response, because we've seen that the stronger the communities are, the faster the recovery process. From a mental health perspective, it's also beneficial. And from just a personal health perspective, it's so much more beneficial. So anything we can do to lower entry into a system and keep folks

in place or with friends and family, the better.

And I think, to your point, if you know a disaster -- a hurricane is coming, wouldn't it be wonderful to say, okay, I've got my portable generator and I'm going to go up to my niece's house 300 miles from here and I know I'm going to be okay? And the issue is not even an issue now. And I think that's what our real goal is, is to empower these folks to be independent and to be prepared and to be able to maintain their status of life and their comfort no matter -- well, I don't want to say no matter what, but as reasonably as possible.

MS. SCHUENEMEYER: And you had one more slide in the printout.

DR. FERRO: Yeah. So this was in the appendix. This is just a pilot diagram. This is what we have. So this was our concept that originally we put together when we first kicked this off, which was to have somebody sitting at home. And this puts everything I just discussed into a nice picture, which is having somebody who sits at home, and they are able to, over a secure communication link, put their device ID, their location, and their current state and time over a number of networks, depending on what infrastructure is available.

Again, if your power is down but your cell phone is working and the network is good, it goes over the cell phone, and it's linked to a secure portal data pilot plot. And folks are registered in there and the data is secure

and all the HIPAA and everything is taken care of. And then that can get fed out to the right folks at the right time; friends and family via social networks, to VOADs and homebound programs and to emergency response. And that's really our thought here, is this whole community approach.

DR. ZABRANSKY: Thank you.

At this time the Committee will now start its deliberations. Again, this portion of the meeting is open for the public. However, they will not be -- they can only address the Committee upon our request. So if there's any specific questions for any of the people that have spoken, specifically the FDA, who have made three presentations, and again for Dr. Ferro, who came from another portion of HHS, please put those -- put your thinking caps on for these last bits of questions.

We've heard before, probably in the past, the adage that "I'm from the government and I'm here to help you." Well, at this point, we are here to help the government. I hope, anyway.

So let us now proceed with our questions, that we have to at least come up with some thoughts for the FDA to address in response to these questions. We may not reach a consensus on what has to be said, but all aspects of what addresses these questions, we should try to get down.

So we're going to take one question at a time. Is that right, Jennifer? Okay.

DR. KELLY: All right, Question Number 1: How should industry

address extreme weather conditions during the device design process?

DR. ZABRANSKY: Anybody want to go at it?

DR. KIMBERLIN: This is Cecilia Kimberlin, Industry Representative.

I think a number of these points have come up already, but perhaps I'll just reiterate some of them to put them on the table for discussion and deliberation.

During the device design process, that's an excellent time as industry has already implemented a risk management process to think about the criticality of this device, how and where it will be used, and under these types of conditions what would be the impact, and build that into the fault analysis and the potential failure modes. You know, if I understand where industry is today, with the exception of probably a few devices, we probably aren't thinking this broadly and this fully.

I agree with comments that came out earlier, that this wouldn't be a "one size fits all" and there would probably be some benefit down the road for guidance where industry could comment back on some draft guidance on how best to apply this.

So that's one thought that I've put on the table.

DR. ARMSTRONG: One question that I have is that it would seem to me that there's a fair amount of competition among device developers which leads to usually a fair amount of costs that go along with

that. So what is in place for there to be crosstalk between the people who are developing these devices, how is that monitored and how are strategies or design or results shared among industry?

I'm a layperson where it comes to device development, of sorts, so I get the end product in terms of devices that we use, but I also know that -- and I'm enough on the ground to know that everybody's competing and whoever comes up with the best device then sort of gets the money and that those costs are passed down to the consumer.

So in our zeal to be able to develop superior devices on the front end, where will the cost controls be located and who will oversee that? And what, if any, role does the FDA have in that?

DR. KIMBERLIN: Well, Dr. Armstrong -- this is Cecilia Kimberlin again speaking.

I think you make a very excellent point, and it's obviously clear that companies are in competition, and there are proprietary issues that we already deal with. But I think when it comes to the threshold of safety and effectiveness, we all have to strive to meet that essential entry point, if not do better, and that's where the competitiveness comes in.

So if there were guidance to industry and a consensus among the industry that for particular types of devices we would take this approach to make sure that they safely and effectively can operate in extreme conditions, then we elevate the entire industry. And will it add cost?

Probably at first, but we're very innovative in terms of trying to get cost out. I think there's a lot of data out there --

DR. ZABRANSKY: We're trying -- just try to stay away from, you know, what it's going to cost.

DR. KIMBERLIN: Yeah. Cost, right. Exactly. Good point.

But another factor that I'd like to give you an example of, of how we've learned and worked together -- and the Agency has been very helpful on this -- probably it's been a decade ago, the head of the IVD group, Dr. Gutman, pulled industry together; we took a look at the outcomes in terms of hazard analysis for glucose meters, what is industry reporting. Not everyone was consistent.

And he pulled an industry forum together, and we had good discussion. He made the data very generic. He didn't identify any particular device, but we were able to come to a consensus on the type of safety issues that were out there and we're dealing with. You could say, well, that's after the fact, but I promise you, every company in that room went back to their design group and said we can do better.

So it again not only made the postmarket part much more effective in reporting, but it really influenced the next generations of glucose meters coming forward. So there are ways that we could use existing data and pull people together. Each company went back and had their own innovative way of addressing those issues. But I can promise you, if they're in

competition today, they address those issues then.

MS. BLACKWOOD: This is Liz Blackwood, Industry Representative.

I also worked for a couple of years in the blood glucose monitoring business, and I think Steve Gutman had just gotten into his new role at that same time.

And one of the things that occurred during those couple of years was that, for those of you who don't know this, blood glucose meters are only plus or minus 20% accurate, which sounds crazy if you're on insulin. But that was a fact. That was a technology, that was a limitation of the electrochemical reaction and so forth.

And at one point in time, one of the competitors came up with plus or minus 15, and it was pretty effective. And whatever it cost them to do that, whether it was calibration during manufacturing or a new chemical reaction or new electronic accuracy and precision, whatever that was, that became FDA's new benchmark. And so when you'd come in and say I got an equivalent meter -- no, you don't, was the answer.

So FDA helped industry to raise the bar, and then it was fair, right, versus why should I have to do that. Well, you know, you probably want to do it, right? It's better for the patient, it's -- but it costs, it costs. So it does help industry to create that level playing field.

I think, just on a very different note, the engineers are really

smart, but they're also very good at following a process. And my experience is if the process doesn't spell out to think about it, they're going to kind of engineer it to meet the common circumstances. So I don't know if many of you remember back in the nineties when we were looking at process validation, it talked about the parameters Jan talked about this morning, you know, like what are the worst case conditions.

Well, a few years later we added in the concept of "and what unintended consequences may occur," now you have to address those and the engineers are like oh, okay. Unintended consequences. Gee, now maybe I need to modify my process a little, make it a little tighter; even though I can operate out here, maybe I should operate in here.

So I think if we put things, like, for -- call it Class III devices, call it life saving/life sustaining devices, however we decide to target what we want to go after, if we say to the engineers it's required that you consider the extreme circumstances associated with disasters and emergencies, they'll do it. And if everybody in the industry is doing it, all of a sudden it's awesome, right? It's like, ooh, we can do it this way/we can do it that way versus we're going to be the one company that goes above and beyond, but we didn't really even think about it.

So you're making us think today, right? We are making each other think. But it hasn't kind of been in the cookbook up until now, right? So I think if we added in, whether that's through temporary guidance

documents and eventually comes to the reg, whether we do it through risk management or in the classification of devices, I think it will force the technology and the competition to make it more interesting and higher quality.

DR. ZABRANSKY: Ms. Fiore, do you have any thoughts on -- again, we're addressing what industry should be doing to address the extreme weather situation.

MS. FIORE: Well, certainly following through on what Mr. Ferro just outlined, I think that that's the next generation and it's where the answer to the disaster response lies. In the meantime, I think that most of our -- as far as oxygen is concerned, we depend upon the fire departments because they have a ready supply. But as I said, this new department seems to be moving forward rapidly and in the right direction.

MS. SCHUENEMEYER: Terry Schuenemeyer, the Public Respondent [sic].

I think that I agree completely with what Ms. Blackwood was saying, is that if it's not in the process, the engineers generally aren't going to do it because they do follow -- they're very regimented and they do things exactly the way that they've always done them and they're very good at that.

So if we were to make distinct suggestions of what they should be doing, whether it's increase the bar on the design so that it incorporates a better design to protect these devices, whether it's labeling, packaging,

transportation, I think that putting it in a guidance will be very helpful, but putting it in the regs is where it's going to end up finally happening.

DR. ZABRANSKY: Steve, you had a question?

DR. McNAMEE: Scott McNamee, CDRH.

DR. ZABRANSKY: Scott. Excuse me.

DR. McNAMEE: Speaking as an engineer, I appreciate your points, and they're very well taken, and I'm going to ask for some concrete guidance from the Committee. I've heard that this sense of guidance documents would be very helpful. I think what would be most helpful, from the Advisory Committee, is a sense of which direction such actions you would recommend to pursue first.

Would it be a guidance document for all Class III devices; would it be a guidance document for all home-use devices; would it be a guidance document for all life-sustaining devices that are mobile; would it be for all devices, period?

If it pleased the Chair and if possible for the Committee to kind of come to a sense of where you think the priorities ought to be, those kind of recommendations would be, I think, most helpful to the Agency.

DR. ZABRANSKY: That presents another issue.

There was a question over there, first. You want to wait or --

DR. ARMSTRONG: I have a question. I made a point of writing down something, I think, that you said -- maybe it was someone else -- about

the fact that component suppliers are not subject to FDA controls; is that correct? Did I write it down wrongly?

MS. WELCH: This is Jan Welch.

Can I help clarify that?

DR. ARMSTRONG: Okay, yeah.

MS. WELCH: Okay. So I think it's the component manufacturers themselves do not have to comply with the Quality System regulation. However, the finished device manufacturer has to control their component suppliers through the purchasing control provisions in the Quality System regulation.

DR. ARMSTRONG: Okay.

MS. WELCH: So there is control.

DR. ARMSTRONG: It doesn't get dropped.

MS. WELCH: No, ma'am.

DR. ARMSTRONG: Okay, all right. That's helpful.

Back to you.

DR. ZABRANSKY: Dave, did you have something?

DR. CRANMER: I do. This is Dave Cranmer, Government Representative.

I think I'm a fan of guidance documents given that there don't seem to be any extant at this moment. I'd start with a risk stratification document that lays out more or less what you do for the critical, the Class III,

kinds of devices and then work my way down to the "ones" where things are less critical. After that, I think that will tell you what the different branches are that will tell you what you have to do next.

MS. BLACKWOOD: So to maybe put a thought on the specificity around "should we do Class III, should we do life saving/life sustaining," I wrote down -- Jan was talking about, you know, this level playing field, around 50% of manufacturers have less than 10 employees, let's be fair. All right, if it's required, let's make sure we require it to the same type of device and not necessarily everybody at all levels of everything ever known to man.

And I did write down -- and I'll put words in your mouth, Jan, but I think I did pretty well. You said something like, that we should determine what devices are prone to degradation as a result of exposure to extreme weather conditions; could be some semblance of what Steve said, of mobile life saving/life -- something like that. But I think, in a guidance, if we started with something like that and then said these are the categories, you know, process validation, environmental conditions, handling, storage, transportation, and here are the considerations during your risk analysis of your environmental conditions during design, I think -- I'm paraphrasing, but that would be kind of the guidance, right?

And people tend to think, oh, guidance is guidance. With FDA, when guidance goes in, it goes. And it goes out to ORA and the districts come in, and they have it in their pocket and they audit against it. And they're like,

listen, we put the guidance out; if you can't get it right, use the guidance, right? So they don't audit against it, per se, but they certainly expect you to utilize it.

So I think guidance, at least in the United States, has some teeth. In ISO world, not so much. But I think, starting with a guidance document, I think it would be a good way to go. We just have to have criteria around "what does prone mean, what does that mean," and then I think we've already done a nice job of figuring out what areas would we want to have for consideration.

DR. CRANMER: Yes, this is Dave again.

The other concern I have -- actually, a couple of them.

One, the smaller manufacturers are going to be more resource limited, so you don't want to write whatever it is you write in a way that forces them to use way more resources than are available to them.

The other thing I'd be very reluctant to do is prescribe the behavior in regulation because --

DR. ZABRANSKY: Say that again, please.

DR. CRANMER: Prescribe behavior in regulation.

DR. ZABRANSKY: Oh.

DR. CRANMER: Because then I'm going to end up using terms like "use best available control technology" like EPA used with controlling coal plants, and I'm going to get into all kinds of legal and other fights because

"who defines best?" And if I've now got something better, what protocols do I have to go through now to prove it's better than what's available?

So I know enough engineers who are smart people. I think there's more than one way to do things, and they'll figure that out. If I prescribe it in regulation, they're all going to have to do the same thing, and that doesn't necessarily help me be innovative.

DR. ZABRANSKY: Ms. Olivera, do you have any thoughts on this?

MS. OLIVERA: This is Mary Olivera.

I was thinking, probably on the extreme weather rating for devices in which the categories of the products can be aligned along with those ratings based on how critical they are.

DR. ZABRANSKY: Oh, I'm sorry.

MS. FIORE: Edna Fiore.

In line with the ACA and the emphasis on keeping patients away from institutions, I would -- referring to your original question, I think that you should have a definite emphasis on the home situation.

MS. SCHUENEMEYER: Terry Schuenemeyer, the Public Respondent [sic].

I think that the home situation is a good idea, and if we were to say Class III devices, it's not necessarily the Class III implantable device, which may be implanted or sitting on a shelf. It could be more of the programmers

or the associated products that go with it that could be damaged. If it's a device that's sitting on the shelf waiting to be used, those could be sent back and reprocessed.

If it's something that's out in the community, a doctor's office or a hospital, that is going to be relied on to test a critical piece of equipment like a pacemaker or a defibrillator, those could be damaged; and perhaps thinking of a way to protect those from the environment would be a bit of a priority rather than something that's in a package on a shelf that could be put in a box and sent back to the company and say, you know, this was damaged during the earthquake or the tornado.

But the programmer that's sitting there you need to rely on in order to test your patients when they come back in, so that's usually one piece of equipment that you have, not 10 devices sitting on a shelf that some of them may or may not have been damaged. I think that one of the things that if we're going to just say Class III devices, you should possibly think about categorizing which ones are more vulnerable in patient care.

DR. ARMSTRONG: Brenda Armstrong.

And sort of to follow that, it would seem that there's a short-term impact. A life-sustaining device is not just -- I mean, it's immediate versus -- not a pacemaker on a shelf, but a valve, for instance, that's sitting on a shelf waiting for an opportunity to be implanted, you know, that there would have to be some language to sort of help guide how attention to the

impact of a terrible weather event would have on something that is potential versus real.

Someone who is dependent on a VAD at home or an oxygen tank at home or those things that are immediate, it would appear that the clarification or risk stratification for that is going to be different than some of the devices that are sitting on a supply -- as part of a supply cart that is waiting to be used but is really not life sustaining in the sense that has been described by you all and is, by the way, the way we look at it, too.

DR. ZABRANSKY: Okay, I'm going to try to sum up some comments here.

I got the general impression that some sort of guidance document is really what the industry is asking for, despite the fact that we're asking industry how they should do it. Industry is now coming back to the FDA and saying give us some guidance.

Well, they want guidance on, you know, what type of -- what fact or what risk factor or what risk ratio should be looked at by getting high risk and Class III, but yes, also we've heard that may be a home product, the home use or the point-of-care devices.

I think the concept of crosstalk between industry is very useful, again, but I don't know if that can be put into a guidance document. You know, that's --

UNIDENTIFIED SPEAKER: You're not allowed.

DR. ZABRANSKY: Not allowed to. And somebody's right. That's one concept.

One thing that can be addressed in a guidance document, apparently, is that all possible conditions -- someone mentioned, you know, that the product is designed for normal use or a little bit more than normal use. The engineers have to stretch beyond that to the point that all possible problems that might occur. Now, that can be perhaps put into the guidance document.

A couple of times we've heard before about universal batteries. I sure wish we could get Rayovac and maybe Johnson Controls and some of these other companies out there, perhaps, to design some type -- I'm sure it's being looked at. But, again, industry has to be willing to consider the use of a universal battery and not design one. My cell phone battery doesn't fit yours and so forth. That's a real problem.

And the other concept was meant that maybe the issues of weather severity, somehow, should be taken. And I don't know how you measure a Richter scale 8 earthquake against a Class 4 hurricane, I don't know. But, you know, two different situations. But I don't know if that can be incorporated into a guidance document.

Did I kind of sum up what, most of what we were talking about?

DR. CRANMER: Yeah, I think the other thing -- this is

Dave Cranmer.

The other thing that this really addresses is more the management subsystem of the Quality System because these are going to be management decisions about what level of risk -- financial, product, and other -- that you are willing and able to accept. But you're really looking for a more robust plan for your design as well as for the manufacture of your device. I think that's the thing I'd like to see industry address.

DR. ZABRANSKY: Um-hum.

DR. KIMBERLIN: This is Cecilia Kimberlin of Industry.

Dave, I would agree that it's management; that we can build it into the risk management process that is in existence today. And the elevated risks do get elevated review.

When the Agency responded a few minutes ago and we kind of had this banter back and forth -- industry wants guidance and the Agency wants to know from industry more specifics -- in terms of this question for the device design process, we do have a risk management process in place. If we could enhance that risk management process, through guidance, looking at this device that's being designed or redesigned with the questions added from the guidance in terms of these extreme conditions.

Right now we're talking about weather, we're talking about interruptions in supply, extreme conditions to the product, and build that into "these are the hazards and the possible failure modes" that we need to think

about, where in the past we may not have thought about. If we could target that area, I think that, you know, the industry is pretty savvy in terms of "is this a critical device, is it going to be life saving." We maybe don't have to specify that, but those questions can be answered in the risk management process.

So I think there is a way to tier this so it's not very complicated, and small and large industry can take this, and based on the type of device they're designing, again, with the flexibility that the Agency has provided us to make something like that work. And industry would, I think, be very interested in if the Agency wants us to provide some initial thoughts on this, that we could get groups together to provide some thoughts around how we'd like to see this shape up and then -- or else you guys could draft it and we can respond or we can help with it.

DR. ZABRANSKY: You've heard some more suggestions and concern. Now, is this -- do you want further discussion on this issue, or do you think we're there? Or not there, but --

MS. WELCH: So this is Jan Welch.

So I'm listening to this, thinking "guidance document, how to write this" and wow. And I'm thinking of all of the vehicles that we already have out there that FDA has available that we've drafted in the past. So we do have -- I won't say it's a "recent guidance document," but we do have things that we published in 1996-1997.

I'm immediately thinking, in the back of my head, about GHTF and all of the work that GHTF did in Study Group 3 with integration of risk management in the quality management system. One of the last documents they drafted was the supplier controls. So it's like there are things already there, so I'm sort of listening to all of this, thinking it's like reinventing the wheel or starting from scratch or oh, my gosh, starting all over again and writing this, and I think we've got some vehicles there that we could go back and look.

And it goes back to what Liz and Cecilia, you've been saying, a lot of it is being done. It's a little bit more; it's what I said, it's going to that next step and a few more considerations, so maybe we go back and look at what is already extant and see okay, what's the delta, what's the gap, because I personally just don't think there's a need for brand new, start-from-scratch guidance because we did this, you know, when the reg came out. We've done this in the last eight years cooperatively, with what was then GHTF. So we don't have that exact same vehicle right now, but those documents just don't go away.

So those are the things I'm kind of thinking about that maybe it's not a creation of a new product, but it's something that we go back and take a look at, what are the deltas, what are the gaps of what's available.

DR. ZABRANSKY: What you're saying is more of an upgrade, maybe changing --

MS. WELCH: Yes, sir.

DR. ZABRANSKY: -- a couple paragraphs, an addendum, or a codicil to the original documents?

MS. WELCH: And putting -- yes, sir. And putting some of that out for comment to all of you on the panel or to industry to say, okay, this is what's -- we flag some of these areas and say, okay, you know, we thought about EMC and we thought about this, we thought about that, but we didn't think about X, so what are we missing? What are we missing?

DR. ZABRANSKY: Okay.

Any last suggestions or comments concerning Question Number 1?

MS. SCHUENEMEYER: Terry Schuenemeyer from -- again.

That sort of falls back to what I said earlier today, when I read the Quality System regulations in preparation for coming here several times, I just kept thinking these are good. These basically say what you're supposed to be doing and possibly just adding a little bit of language that brings to mind, at the beginning or somewhat throughout it, you know, be sure that you have processes in place, risk-based processes in place, to evaluate for extreme emergencies.

I don't think rewriting all of these would make any sense. And maybe that would be in the management control section. The management is responsible for having a plan in place that would address these extreme

emergencies.

MS. WELCH: All right. So this is Jan Welch from FDA.

So I think that we have -- I personally wouldn't see it in the regulation, but I would see it in the other documents that we've created. We have a small manufacturers guide to good manufacturing practice. It hadn't had an overhaul, but it's still -- most of the information that's there is relevant, but it goes through this kind of upgrade.

So yeah, I'm just thinking that I could go back to my office and pull 10 documents that FDA has authored on design controls that touch on the QS that maybe need just a little bit of this additional consideration with what are today's, you know, 2013 sort of state-of-the-art challenges that maybe weren't considered or fleshed out or really at the fore in 1996.

DR. ZABRANSKY: A question for refreshing. You take a guidance document that you just mentioned. Supposing you go through it and you make your revisions. Now, what is the issue on open -- what do you call, when it's open for discussion, for comment, for public comment. What's the timeframe involved and so forth, again, on those?

MS. WELCH: That's a great question. So this is Jan Welch from FDA.

It depends on what the document is. None of these that I'm thinking about were really issued as what we would call guidance. They were reference publications that we generated. So that's a different model and, of

course, back in 1996 we didn't have the level of good guidance practice scrutiny that we do today in 2013. So it's a great question, but perhaps, again, we're not talking about voluminous changes.

DR. ZABRANSKY: Right.

MS. WELCH: I just don't believe that. I know what has been written on risk management practices, and the delta just isn't that big.

DR. KIMBERLIN: Jan, I think Liz and I very much concur with what you're saying, and also I think the approach that you're describing would be very well received by industry. This incremental enhancement of what's existing is exactly what we need.

MS. SCHUENEMEYER: I think that we -- Terry Schuenemeyer again.

I think that we've sort of jumped from Question 1, which is just talking about device design process to a discussion that's talking about the entire process and sort of incorporates all of the questions.

And I think that they all could be put into this format of the regs may be fine, but tweaking the other products that are used to guide industry and maybe with focus on the Class III devices or maybe with focus on sole manufacturers or using the risk-based way of deciding what emphasis should be put into any revised documents or guidances to focus on the different areas that we've heard information on today that might be the higher risk.

And the production and process controls, device design, environmental controls, all of these are already discussed in the regs, and if we add things to the other documents, then maybe we should talk about prioritizing where their design changes would be.

DR. ZABRANSKY: Okay, we move on to Question 2, which really addresses specific regs, which is the Quality System regs, 21 C.F.R. Go ahead.

DR. KELLY: Question 2.

DR. ZABRANSKY: Oh, I'm sorry. Excuse me.

DR. McNAMEE: Scott McNamee, CDRH.

From what I'm hearing in the discussion, it sounds like -- and I think -- no, I know I support what's being said because it makes good sense, that what we've done is, I think we've highlighted a change in the risk space that industry and the Agency are all working within to try and protect the public health.

And I don't want to put words in the mouth of the Advisory Committee, but it sounds like what you're suggesting is revisiting what's already out there and make sure that it's up to date with this new information with regards to that risk space, what is new, what is the delta due to extreme weather events. What are the other risks that fall out as a result of that change, and how can they be addressed in a way that helps the industry create a better product to protect the public health without being unduly burdensome.

So not a rewrite, but a relook at in light of the changes that are happening in the environment and the changes that are happening in the marketplace, what's the most efficient way to address those is one of the things that I'm hearing in terms of your summaries.

DR. ZABRANSKY: Okay, Question Number 2.

DR. KELLY: Number 2: How might Production and Process Controls from the Quality System regulation best be applied to ensure the safety and quality of medical devices that are affected by extreme weather events?

DR. ZABRANSKY: Any comments now on this? We'll start over on this side.

DR. CRANMER: This is Dave Cranmer.

I think this is an area in particular where my concerns, because of the increasing number of extreme weather events, might go beyond what FDA would specifically require under QSR, and that's to work with the facilities' owners and managers, to think about to the extent it makes sense, having not duplicate facilities, but alternate facilities to produce critical devices. And I think I'll leave it at that.

DR. ZABRANSKY: Dr. Armstrong, any thoughts?

DR. ARMSTRONG: No.

DR. ZABRANSKY: No, okay.

DR. ARMSTRONG: I don't think so.

It all still goes back to some sort of stratification of risk and then applying best practices to those devices or those situations that have the highest risk, and it sounds -- and in looking at the regs, that it's more taking the frequency and severity of the events that are occurring and applying some urgency to the creation of, or the modification of, what's existing now.

And those weren't terrible, to start out with, so we're not starting out at zero; we're starting out at 70 hoping for 100%. And it would seem to me that a review of the devices and in terms of some priority is what is more in line and an adjustment to apply those sort of high-risk situations or to review to see if what's available now is reasonable. And it may very well be that -- you know, going back and looking at it in terms of priority will sort of answer the question. Not sort of -- will answer the question.

DR. ZABRANSKY: Mary.

MS. OLIVERA: Mary Olivera.

I was thinking not only process controls on reusable devices and whether or not those devices get contaminated in extreme weather, and whether or not manufacturers can give specific instructions on how to decontaminate those devices and test and put them back to use or reprocess devices that have been contaminated so it's not a total waste on those things.

MS. BLACKWOOD: That's very scary to manufacturers. We don't really like to reprocess because we'd rather give a new one that's been

tested under our control. There are capital goods that have refurbishment and servicing processes that are validated and prescribed as part of the design in the installation manuals and user manuals. But if those are not available, generally devices need to be returned for repair or replaced.

So where I thought you might be going -- I'm sorry, this is Liz Blackwood, Industry Representative -- was that in 820.70 P&PC and then in 820.50 storage -- 150, excuse me. If you took those together -- so that's about production, environment, and warehouse environment, and if you put those together for the work that you've already done to maintain your manufacturing environment and maintain your storage environment, and gave that to the hospitals and the distributors and said this is how we handle, preserve, and store our stuff per the labeling, it might help, right, to say here are your conditions. Because what we do is we really put the expiry date and whatever is required absolutely on the label versus this is how we, you know, transport and so on and so forth. So that's one way I think we could use P&PC.

And I'm not meaning to pull your idea, sorry. I was just thinking about if the user has a problem with the device, I'd rather have them call us and we'll fix it instead of giving them instructions on how to do that. They can be quite sophisticated, and upgrades may be available in terms of software, and we would want to reset them to whatever the current version is.

DR. ARMSTRONG: Brenda Armstrong.

How rigid are those? I mean, how rigid are those requirements? Say, for instance, a catheter or aesthetic catheters, are those -- is there any -- you know, a hospital is going to ask should we just throw them out if we basically did not either get to or get beyond an expiration date or a set of circumstances for storage. So how rigid -- and I'm really asking for clarification, how rigid are those restrictions, and is there some guidance that is given for storage or some flexibility?

Because the folks who have to oversee that on the other side, on the side of hospitals or users, are going to see January 31st, 2014, and if it's still there on February 1st, the question is, are we within our rights to keep it, and if not, I think those are the kinds of things, having had to stock a cath lab, that we're throwing stuff out.

MS. BLACKWOOD: Yeah. It's very strict. I mean, it's -- in part, it's -- Liz Blackwood again, Industry Rep.

The expiration date is not just associated with the degradation around age and conditions or the active ingredient, coating, if there is one, but it's also associated with the sterility of the device and all of that is taken into account when we come up with a shelf life. So you would -- yogurt, I'll eat it three days later. My husband thinks it's crazy, but I do. But a catheter, I wouldn't use it after the expiration date any more that you'd take a pill after an expiration date. You just wouldn't do that.

And typically those devices that are -- that feel like they're not durable or capital but they are labeled as reusable, they absolutely come with validated instructions, which we go through a very rigorous process around how to not only clean, but disinfect and/or sterilize if it's required, depending on where you're going with it. You have to sterilize it, right, so --

DR. ARMSTRONG: So that data -- this is a terrible use of words -- is a drop-dead date. It's not negotiable at all.

MS. BLACKWOOD: You know, there are some devices like maybe a knee. There's nothing dynamic about the knee. There's no coating. It's probably not going to degrade even if you buried it in the dirt, okay, but it's sterile. So sometimes we can -- you could call the manufacturer and say hey, it expired, and they say, well, send it back because we can reprocess it and we'll just give you a free one. So there are some things like that, that are robust enough for us to reprocess, but if it expires, I'd call the manufacturer or throw it out. Call the manufacturer first; you might get a free one.

DR. ZABRANSKY: Yes, there are a number of laboratory devices that you cannot use them past the expiration date because of the chemistry involved in them. I don't care what part of the lab you're talking about.

MS. SCHUENEMEYER: I think in Question Number 2, there are different aspects to look at.

One is, if there's a product that's been shipped, it's sitting on the shelf, it's in a hospital that is affected by an extreme weather event and

perhaps they're out of power for a certain amount of time, it's in an area of Puerto Rico or Houston, Texas that's hot and humid, and I think that for the process controls and the company that manufactured that device could possibly provide those affected hospitals with information to help them gauge what should we throw away and what can we keep.

If your product was sitting on the shelf -- or flooded, obviously you're going to throw it away. Fire, it's probably destroyed. But the possible contamination because of extreme heat or humidity changes is more subtle, and perhaps guidance from industry to affected areas as to what to get rid of and what can still be used might be helpful. Or just send it all back and we'll replace it.

But the second part of it is, a manufacturing facility that is in Gulfport, Mississippi that is hit by storm surge or hit by high winds or has a disruption to the water supply, what type of processes will be required to get back on line for the manufacturing facility, and what would we expect them to do to test their new water supply, to validate their humidity controls, their facility, before they start manufacturing again or before they ship any product that was in process.

Perhaps they have things that are halfway through the process when the event happened and they lose power for two weeks. Do we expect them to scrap what they have started or what -- that is not specifically discussed in the guidance how severe we would -- or what severity we would

feel comfortable with of industry going back and starting up again, what type of decisions would we want their senior management to make.

I think that that's the second part of it that this group is being asked to look at. And I believe industry is going to follow the regulations, and I believe they're going to follow any guidances that come out of this meeting. I think that part of the guidance should list maybe the things that FDA or the public would expect them to consider reevaluating or -- before they turn that process back on.

DR. KIMBERLIN: This is Cecilia Kimberlin, one of the Industry Representatives.

You raise very good points, and let me take your second point first, and that's the one of in-production interruption. And that's something that industry has been dealing with. Maybe the types of interruptions have been different, but in essence you're going to have some kind of event that interrupts production unexpectedly or even you expected it and it's worse than it was.

So I think the regulations that are in place, when applied appropriately and by compliant and quality-minded firms, work very well. The decisions, the way the events are documented, the way the investigations are performed, the way the material is contained and not distributed, as we said earlier, there is often data beyond the validated ranges where you have design of experiments and you can make risk

decisions based on that, gets reviewed by a multifunctional team.

Certainly, we all understand it would be under the review of the Agency when they come in. And in such an emergency event, we would expect to be talking with them in our district office or the center. In high-risk devices, this type of manufacturing process is actually looked at before the product is even approved. So I think there are adequate things in place.

You know, one of the things is just to make sure that industry is approaching this on a level field is what we talked about earlier, like Jan said, to go in to those points of existing documents and make sure that people are thinking this properly. Because I'm not sure that if you haven't gone through the tsunami experience, the Hurricane Katrina, the Sandy, and you haven't really understood it because when we've gone through it in the large company where I was, you know, we had a crisis management team and we sat down and reevaluated after each event what could we have done better, how could we have communicated better. So any of that lesson that's been learned -- and I'm sure your company, Liz, has done the same thing and many others, many of them are out there doing it.

Part of my thought about this whole committee meeting is how can we share -- and I think there was a question that asks that later, how can we share these best practices. But my feeling is, and experience is, that the regulations and guidance that are in place give us adequate direction and understanding of how to manage this.

DR. ZABRANSKY: Yes, the question here really does apply to the QS regulations, not to the guidance that's associated with it, and I hear you saying that you think they're adequate. You don't think they're adequate?

MS. SCHUENEMEYER: No, I do. I think that they are adequate. I think that we need to think about raising awareness and not necessarily at the large companies, because I'm sure you do have a lot of crisis management in place, but perhaps the smaller companies would be a focus where they don't have this advantage in place.

And I think that one of the things that might be thought about is the compliance department might want to focus on the smaller companies as opposed to the large companies which have experience and have personnel and have processes in place, that you may want to focus on some of the smaller companies that are producing critical devices. Would they know what to do, how to test the water supply?

MS. WELCH: This is Jan Welch from FDA.

I think so. Because these manufacturers, albeit they're smaller, 5 people, 10 people, they've submitted a 510(k) or a PMA to the Agency, so they've established a quality management system, and unless they haven't particularly -- well, clearly, if they had a PMA, we went out and did a preapproval inspection before the product was allowed into distribution. It could be possible for a 510(k) device, that we have not gone out and done an

inspection, but generally we will have done an inspection with some degree of frequency.

So they know about the regulation, they're compliant with the regulation, so they understand. They don't have to have the same elaborate structure that a larger manufacturer does, but they have to have some mastery of this and some understanding or their device wouldn't have been cleared, approved, or allowed to be distributed in the first place.

DR. ZABRANSKY: Go ahead.

MS. SCHUENEMEYER: Terry Schuenemeyer from Public Response [sic].

I think that that's good input. I think that's great. So that it's sounding more to me like the regulations don't need to be changed, that perhaps the guidance platform would be a better way to go.

MS. WELCH: So this is Jan Welch from FDA.

So the one thing I just want to say, too, is I think that -- and industry appreciates this when FDA says this: "You know your business better than we do, you know your plants and facilities better than we do." I mean, yes. We have many experts at FDA in many different things, but you're the master of what you develop, what you design, and what you distribute, so that I think that as an agency, we've put out this basic, basic requirement to the Quality System regulation, but your daily quality system is what will have these requirements in place for your daily, weekly, monthly operation.

You know you're going to have problems that are minor in nature, in a way, compared to a tsunami or an earthquake. But I said it before when I was talking about my slides, there are manufacturers out there, you come in, you know, roofs cave in, your aseptic processing goes down, your terminal sterilizer doesn't work. I mean, you have these problems and you deal with them because that's what your Quality System is designed to do.

So I think it's by and large my thinking that industry knows what it needs to do, you know, when a facility goes down, when you need to bring it back up, when you're transferring to a new facility, you've got all of that, and I kind of hearken back to, "Okay, well, then in the event of these incredible events that we're not thinking about, you know, happening tomorrow, what are we not quite prepared for?" I think day-in and day-out, it's working.

MS. BLACKWOOD: Liz Blackwood, Industry Rep.

So totally agree, Jan. So I guess the point in Number 2 would be how do we take our very clever monitoring mechanisms and controls that we use in manufacturing and we use in storage, and communicate those to the use community, be it house and so on.

And if you notice, like your ketchup says keep refrigerated after opening, but your ham says here's safe handling instructions, so maybe some devices just say keep it at ambient and other devices say keep it five feet off

the floor, unplug it at night, you know, reboot it after -- whatever. So does that make sense?

DR. ZABRANSKY: Okay, to sum up. I guess what we're hearing is that the current state of regulations, at least as far as a quality system approach, seems to be adequate and -- but perhaps, as a concern, or somehow -- I don't know if it can be put into guidance, I don't know if you have to change the regulation, just to add that industry has to do a better job of informing the user, perhaps with -- if that somehow can be put into guidance.

Is that -- maybe, you know, I don't know if this addition -- if you change labeling, then we've got another issue. If you have to add it to the labeling of a particular product. I don't know.

So okay, now -- excuse me. You folks kind of satisfied with these responses here? I think you would be happy that you don't have to change the reg specifically.

MS. WELCH: Well -- this is Jan Welch from FDA.

So, again, with respect -- so this is 820.70(a) through (i) in the regulation on production and process controls. If the recommendation is not to change the regulation, then are there specific elements that you're recommending that we highlight, going back to prior guidances or something that needs to be considered? I mean, give us the specifics, I guess, is what we're looking for with respect to production and process controls.

DR. ZABRANSKY: Well, I guess the specific that I heard a couple times here was, you know, that the information that the manufacturer uses in the production and their storage isn't enforced down to the distributor as well as to the user.

MS. BLACKWOOD: Liz Blackwood, Industry Rep.

So Jan, I would say 820.70(c) environmental controls, and then 821.50, which is not P&PC, but that (a) and (b), which is the storage section -- and then as we establish those for our internal facilities, how do we take into consideration how we share those with the storage facilities outside of our control, including the user facility? So 820.70(c) and 821.50(a) and (b).

DR. KIMBERLIN: Well, another point of view. This is Cecilia Kimberlin, Industry.

Another point of view on this might be that if we go back to the thoughts around Question Number 1, if our design inputs are articulated correctly with the right risk management consideration based on the risk of the product in these kinds of conditions, then we would have design outputs that would fulfill those, including the labeling.

So let's take the scenario that we have a critical device that we have identified and designed that under extreme conditions would be very vulnerable. Then could that be translated into the design outputs of making sure that our customers -- and our labeling adequately warns about that condition or if we have mitigating steps to take for the customer, we would

again put those in the design output.

So, again, I would go back to the condition that the design control requirements and the production and process control requirements are adequate. It's just giving this kind of enlightened approach of this incremental increase in risk.

Scott, I like the way you helped articulate what's different today than it was in 1998 and the difference today, that I think Dr. Kelly also addressed, was look at the number of disasters and how far-reaching they are and look at the complexity of the supply chain, the production, and even shared design that we have today that we didn't have when the regs were written.

So I'm trying to think of it in the context of what's different today and why do we need something -- and do we need something different. So, again, I think part of what you're suggesting in this enhanced labeling, which I don't have any problem with, if that's what the product requires, should be met through design process.

DR. ZABRANSKY: Ms. Fiore, do you have any other comments on this or -- okay.

Mary? No.

Dr. Armstrong? No.

Okay. Again, now are we satisfied with, kind of -- I would use the word satisfied. Is this answering some of the questions or the issues?

(No audible response.)

DR. ZABRANSKY: Okay.

DR. KELLY: Question 3: How can Environmental Controls be applied to device production, transport, and storage to ensure that products remain safe and effective during and after an extreme weather event?

DR. ZABRANSKY: Okay, we're going to start all over again here. Some of this we've already -- you know, this is all related. No doubt about it.

DR. KIMBERLIN: Yeah, it is.

DR. ZABRANSKY: Cecilia.

DR. KIMBERLIN: This is Cecilia Kimberlin, an Industry Rep.

You know, one of the things I think we can think about here is there's been a lot of activity in the last decade on supply chain management. I think it was brought up by -- one of the audience members earlier commented on this. And, you know, good distribution practices, perhaps there's something to tie in together in terms of good distribution and storage practices.

So maybe, Jan, you can help me out here that, you know, do you think there's an opportunity -- I know the pharma side has worked very heavily on this in terms of enhancing the control, the supply chain, temperature during distribution, cold chain distribution. Do we think medical device is at that same level? Does it need to be -- you know, that would be an area I would poke at under this question.

DR. ZABRANSKY: Mary, do you have any thoughts on this?

MS. OLIVERA: Mary Olivera.

When you think about packages, say a catheter kit that comes in already sterile and during transport has been exposed to extreme heat or moisture. When we get it, where so many are completely sterile, because we can't see inside that package. In sterilization, we have integrators that we put it in the package, and when it's opened, the nurse can see whether or not the package was exposed. And nowadays we have Class 5 integrators that tell us whether the parameters were met, and with certainty, almost 99%, 99.9, that package is sterile because an integrator is almost as good as a biological indicator.

These kinds of packages, especially things that are critical, had like a thermal indicator in the package. When I get that package, I am certain that the integrity of that package was not compromised; whether it went through whatever conditions, I'm always going to be sure that the package is good because I have a visual that is going to tell me so.

MS. BLACKWOOD: Liz Blackwood, Industry Rep. So --

DR. ZABRANSKY: Excuse me, I was going --

MS. BLACKWOOD: Oh, I'm sorry.

MS. SCHUENEMEYER: Terry Schuenemeyer.

I think that the main thing about this question is the transport and storage, primarily the transport. If something is damaged due to an

extreme weather event while it's being transported, like Ms. Olivera said, the end user may not know it. How do we know if it sat on the side of the road because the truck driver couldn't get to where he needed to get in a truck that ran out of gas and its air conditioning system failed?

The trucker may not report that and it gets to the end user, to the hospital, to the patient; this could also be something that's discussed in the design, in the packaging rather than the regs. It could be something that would be an indicator of what type of condition that package had been subjected to. And I think the engineers are very bright and they might be able to figure out a way to do this to alert the end user and the patient that this particular package may not be something you want to use rather than change the regs.

DR. ZABRANSKY: Okay.

MS. BLACKWOOD: Liz Blackwood, Industry Rep.

I was just going to ask Mary, does something like that exist? I know for sterilization it does, but are there, sort of, smaller thermal or hydronic indicators that -- I know there are big ones because we do, for sure, use those for biologic shipping. We ship them with ice packs and all that kind of stuff.

MS. OLIVERA: Mary Olivera.

We use some thermal indicators that we stick on the washer, decontaminator racks, to see whether or not the temperature reaches the

parameter that we set it through, and you stick them, they're like stickers. So maybe that's something, you know, to look into.

DR. ZABRANSKY: Okay. Ms. Fiore, any comment? No, okay.

Let's move over here. Dave.

DR. CRANMER: I don't think I've got anything to add. I think this is all covered in your risk mitigation, and if it's a new technology that you have to find, I think it's out there. And if not, somebody will invent it for you.

DR. ZABRANSKY: Dr. Armstrong.

DR. ARMSTRONG: I want to just ask a question.

DR. ZABRANSKY: Sure.

DR. ARMSTRONG: In the circumstance of a major severe weather event, is there an obligatory time period where the appropriate surveillance is deployed to make sure that all of these inspections occur?

MS. WELCH: I'm sorry, I don't -- this is Jan Welch.

I don't understand your question.

DR. ARMSTRONG: What I'm saying is, with Katrina, where we knew that the hospital is centrally non-functional, there were, I'm sure, devices that were in the hospital under the circumstance of extreme heat. At some point -- and those devices have the appropriate labeling on it in terms of what the limits are within which the device can sit on the shelf, including a date by which, under normal circumstances, they should be used or thrown out, but under extreme circumstances, that's thrown out the window.

So from the point of the event, going forward, is there an obligatory surveillance about those at-risk devices that occurs, and if so, who does it?

DR. McNAMEE: This is Scott McNamee.

I don't know of any obligatory legal authority that calls for such a surveillance.

DR. ARMSTRONG: So it's a good faith -- it's the assumption of good faith of the institution to do that?

DR. McNAMEE: I think, for a hospital or other clinical setting, there are, as I understand it -- I'm no expert, but as I understand it, there are state and local authorities that oversee the running of those facilities, and they may or may not have rules or suggestions in place for how to deal with an event such as that. For the medical devices that this question refers to, those are probably production, transport, and storage so they may already have been purchased by the facility. But once the facility purchases them, we don't go in and make sure that they're storing them correctly. We don't have the authority to do that.

DR. ZABRANSKY: A lot of that stuff comes under joint commission purview, you know, when the hospitals are examined or evaluated every X number of years. Even that examination or inspection process has been cut down.

But I do hear that it's -- what's happening in-between the time

it leaves the manufacturer and it gets to -- and a lot of times these materials wind -- this is the concern, that it winds up that it's being handled through a distributor.

Now, who is responsible for the distributor? Is it the manufacturer? I don't see -- that's the answer.

The other one is the issue, is packaging sufficient? Those are the two.

DR. ARMSTRONG: And labeling.

DR. ZABRANSKY: Yeah. And the labeling associated with it.

DR. KIMBERLIN: This is Cecilia Kimberlin, Industry Representative.

I'd just like to address Dr. Armstrong's point, though, about what happens in reality if that -- and it could be effect and diversion, counterfeiting, it could be a disaster, it could be a number of issues. So as soon as a company is aware of it, typically what happens is that we would contact our local district office and start getting them involved, and then they usually help us get the right authorities involved. Sometimes, depending on the issue, it could be the FBI, it could an investigation branch of the government, or other sources.

In examples like Katrina and others, again, we work not only with people on the ground in the area, but in our other manufacturing locations, those district offices, trying to figure out who could get what

product where. But it was through that kind of communication. There isn't a reg or guidance that says in this circumstance you have to pick up the phone and call each other. It was done because when there is a responsibility in the field for a product that even has the potential to have an issue and you know, as the manufacturer, you're responsible for the safety and effectiveness of that product, you learn, through experience, it's better to get the Agency and your local district involved as soon as possible and work together on it.

So it's not real firm, but it's very commonly practiced. I'm sure, you know, the other companies operate that way, as well. It doesn't address what's in the hospital, but it certainly addresses what's in the supply chain, and usually then it's returned back to the manufacturer for investigation, removed from the field.

DR. ARMSTRONG: Brenda Armstrong.

So the FDA really does not have any responsibility to ensure that that process has occurred at this point. So that's what I'm hearing, right?

MS. WELCH: Right. So this is Jan Welch from FDA.

So I've been listening to this, and I think it's the applicability of the requirements in the Quality System regulation, so in going back to the specifics in the question, that the requirements in the regulation that we've been talking about for production, it would be transport up to the point that it's released for distribution, and storage up to the point it's released for distribution. Those are the requirements that we impose upon the

manufacturer. So that's really -- all of these parts of the Quality System touch that device until the point that it's released for distribution.

And so therefore, FDA goes in and inspects the manufacturer to assure that there's compliance there. But once those products, you know, leave their facilities and then go to the distributor, it's rare that FDA goes to a distributor; we can, but it's rare because we're looking, again, to assess the manufacturer's control over the point up to distribution. But then once that product, those finished devices, leave the finished device manufacturer and the distributor, the Quality System regulation doesn't -- unless it's an installed -- maybe a major piece of equipment that's installed, but that's where the regulation stops.

DR. ZABRANSKY: Obviously, this does not apply to a product that goes directly from the manufacturer to the user; it's the distributor. And I don't know how often that occurs. I mean, I can think of a number of devices, you know, that there's a distributor as an interim.

And I don't know, again, if the FDA -- can their actions be extended to the distributors? I don't know.

It's just another -- you don't have enough energy or resources to do inspections -- I hear that we have difficulties doing that -- without going out and looking at every distributor out there, as well.

DR. ARMSTRONG: Brenda Armstrong.

So let me just make sure that I heard it right. So the

distributor, once it gets to the distributor, the FDA is then off -- I hate to say it this way, off the hook or -- and the reason that I bring this up is that if there's a distributor that's there and they're holding a set of devices or anything else, you know, especially if they're in that Class III and Class II area and once they get in the hospitals, the JC, the HO, but then there's that gap. Who deals with the distributor?

MS. WELCH: This is Jan Welch.

I'm going to put this back to the manufacturers, the set of controls they put in place for their distributors. And, again, I kind of use the phrase, you know, not all distributors are created equal, right, so I mean there are some that it's one stop, it's one device to one distributor and on. You know, some distributors are huge. So it depends on the nature of the device, how many, and that relationship with the distributor.

And so clearly, where FDA comes back in again would be, you know, yes, there can be a problem with something in distribution; yes, a storage condition. And then the user is going to report it back to the manufacturer, and then FDA is looking to assess what is the manufacturer doing with that information, again, back into their Quality System to assess that information.

DR. KIMBERLIN: Right, Jan. This is Cecilia Kimberlin.

So the manufacturer is responsible for the whole product life cycle. So the QSR, which we're discussing today, gets up to this distribution

point. But we have postmarket responsibility. So from the time it leaves us to get to the final consignee's hands, you know, we have put specifications and requirements in place and we manage our distributors.

At that point where we determine or are aware that something may have gone wrong and there is either a real or potential field issue of product quality, then we have other regulations we follow which, where we determine that does this need to be reported to the FDA and if it's a safety issue, it does. And in most cases, we do end up reporting it and then work under other sets of regulations to make sure that the product is either removed from the field, corrected. You know, there's sometimes a requirement to do 100% reconciliation of every unit of that lot, things like that.

So there are very strict requirements in place for that scenario, and I think that would apply in these extreme weather conditions, as well. It's probably just going to be more challenging to have it happen if everyone's under these extreme conditions.

DR. ZABRANSKY: Yeah.

MS. BLACKWOOD: Liz Blackwood, Industry Rep.

There are many flavors of distributors, right? So sometimes we have our own internal distribution warehouses, in which case that happens to be an extension of the manufacturer just because it's down the street or in a different country, and we're responsible for it until the first point of

consignee.

But to Cecilia's point, we are responsible for the life cycle of postmarket. We have to respond to all safety issues, part of complaints, and resolve them. And so what we've learned is that even though we want to treat the distributor as a customer because we change financial books, right, so we sell it to them and you want to do this, but we've learned that you can't because even though we've given it to them, it's like you give your car to your kid, right? You still want to, you know, pay the insurance and so on.

So the distributors now, we've learned, probably over the last 10 years, you've got to put -- we call them distributor agreements. So we used to think are they suppliers, are they customers, how do we deal with them? And it's like well, regardless, we want to have control over how they handle our products because to us, it's really important that it's safe and effective when it gets in the hand of the user. So quality agreements are put in place. It never says it in here.

DR. ZABRANSKY: Um-hum.

MS. BLACKWOOD: It only really says we have responsibility, the first point of consignee, and FDA only has jurisdiction over manufacturers, including spec developers, blah, blah, blah. So we take it on, we do.

So I don't know if that helps answer the question. We don't just let it rip and nobody knows what happens after that, I promise you. But it's been a struggle because it does change financial hands, and once it does,

there's a sense from the distributor that, well, hey, it's my stuff. And there's no oversight there, from what --

DR. CRANMER: But if something goes wrong, you're still on the hook financially and reputationally, so it's in your best interest --

MS. BLACKWOOD: Yeah.

DR. CRANMER: -- to pay attention.

MS. BLACKWOOD: And we do, yeah.

DR. ZABRANSKY: You know, the issue is that you hear that this might be the case for some of the large manufacturers but, you know, small manufacturers may not deal -- wouldn't want to deal with a distributor, anyway, because it would be more costly for them. It would be better off if they were able to sell direct.

I guess I would wonder if the FDA, when they look at this particular portion of the C.F.R., the regs, is the wording adequate, that all manufacturers will carefully look at their distributors, as Ms. Blackwood is suggesting.

MS. WELCH: So this is Jan Welch from FDA.

I would say yes. It doesn't -- I mean, you know, when you read the Quality System regulation, it just says manufacturer. So the preamble, if you go into the preamble, not so much with respect to distribution or that particular element, the preamble does call out some very specific comments that came back in, in 1995, when we had the proposed rule out, they're

saying how can you, FDA, apply this particular requirement to a small manufacturer, and we responded to that.

So I would say yes, regardless of the size of the manufacturer, we're expecting -- I mean, they're not making as many devices, so they should -- they have the control, the same system. The same system elements need to be there.

DR. ZABRANSKY: It would also appear that the problem reporting issue, if you had a recall, before that recall occurs, a laboratory or a hospital or a user has a problem with a product, they do not go to the distributor. They do, as a rule, go back to the manufacturer. And at that point, it might take a little bit longer to find out where the problem occurred, but it still will be rectified.

Okay, we addressed this issue to the satisfaction of the FDA?

One last comment.

DR. McNAMEE: This is Scott McNamee.

I have a clarifying question. Does industry usually consider the distribution chain as a service that they're purchasing, and would the purchasing controls be part of how those distribution contracts are written?

MS. BLACKWOOD: Liz Blackwood, Industry Rep.

We really don't pay them to distribute our product, so we don't ask them for service. We sell it to them.

DR. McNAMEE: Okay.

MS. BLACKWOOD: And then they distribute it. But we do treat them like suppliers. They didn't like it at first, okay, but they do well. They have a great business around it, and they have faster and better transportation methodologies and channels, so they're experts at that, and we're experts at manufacturing and design, so we've kind of come to a common ground that says you've got to follow these rules; we need to know where the product is going.

Even though the reg says you have to have traceability to the first point of consignee, that doesn't help us when something happens, right. We need to know where -- and Phillips stood and said we don't know where these devices are. I mean, that's kind of scary, right? We want to know where they are, so we build ID and trace right into these third party contracts. So we do have distributor contracts with them, and as such, part of the agreement is a quality agreement, and it hits on storage, distribution, transportation, timeliness of returning information to us, service and installation requirements, et cetera. So we do treat them like suppliers even though they're customers. It's kind of a tricky one there.

DR. ZABRANSKY: This issue of the transport was raised primarily by Ms. Olivera and by Ms. Schuenemeyer. Are we addressing those things to your satisfaction in our discussions here?

MS. SCHUENEMEYER: Yes, I think that what industry is saying addresses the concerns. I am rather surprised to learn that the distributor is

the consignee and that technically, based on the regs, does that mean that that's where the responsibility, as the regs are written, ends? It sounds like you don't -- industry does not take it that way, and industry goes the step further.

So if we were thinking of changing anything in the regs, would that be something where -- instead of saying the first consignee, it would be the end user, being the hospital or the patient, which I'm not sure we would want to put that in there because that would really increase the industry risk, but it sounds like there's a disconnect where the regs say it's the first consignee, and if that truly is the distributor, then are we putting the public at risk if the manufacturer didn't take the final step like it sounds like the larger ones certainly do? It's just a question that -- maybe confusion on my part.

MS. BLACKWOOD: Liz Blackwood, Industry Rep.

I would say that we also know, as manufacturers, that the Agency holds us accountable for safe and effective product through the life of the device. And if we choose to use distribution channels, we need to figure out how to do that effectively without compromising safety and efficacy. Fair?

MS. WELCH: Yes. This is Jan Welch from FDA.

Because I think most manufacturers, whether it's maybe not a supplier audit of that distributor or whatever, but depending on, again, the

criticality and the storage conditions, you're going out and taking a look at those distributors. I mean, you're making sure, because it's your name on that product and it's out there, so they're assuring that these distributors are meeting their needs and their expectations. So I don't think that FDA has perceived that there's a gap because -- or that the public health has been put at issue because we are not inspecting distributors.

MS. SCHUENEMEYER: Okay. Terry Schuenemeyer, Public Respondee [sic].

That brings us back, then, to the point that possibly these concerns could be dealt with in the device design process with a process that would notify the end user that this product did experience some bad effect. And it doesn't necessarily have to be an extreme weather event; it could be a broken-down semi on the side of the road.

So maybe, once again, the regs are fine the way they're written and the issues that we have concerns about with individual products being used can be handled in the device design controls.

DR. ZABRANSKY: I'm sorry. I don't know why that would be part of the design of the product.

MS. SCHUENEMEYER: Well, I'm --

DR. ZABRANSKY: Am I off base on that or --

MS. SCHUENEMEYER: I was referring to possibly building something into the design of the packaging --

DR. ZABRANSKY: The packaging --

MS. SCHUENEMEYER: -- that would notify the end user that there was a problem that had been -- that could have affected this device.

DR. ZABRANSKY: Well, again, it's like the pill bottle that you open now -- we got it difficult for people with arthritis to open it, but then they open it, they still got another layer on there to open.

At this point, it's two minutes after 3:00. Let's take a 15-minute break. Let's resume at 20 after. Promptly, please.

(Off the record.)

(On the record.)

DR. ZABRANSKY: I'd like to resume.

And now we're moving on to Question Number 4, right?

DR. KELLY: How can Purchasing Controls be optimized by manufacturers to prepare for the event that component manufacturers may be affected by extreme weather?

DR. ZABRANSKY: Let us start over here on the left.

Dr. Armstrong, have you had enough time to think about that question?

DR. ARMSTRONG: I hope so.

Well, since I just found out that the end users really are, in a significant way, dependent on the distributors who, in turn, are controlled by the manufacturers, I'm not sure that there are purchasing controls that can

be any further optimized at this point. I mean, I was assuming that the FDA's purview extended to the distributors, and obviously that's not the case, so I'm not sure that there's anything more to be added at this point than what is presently available.

MS. WELCH: Could I just add one little point of -- this is Jan Welch from FDA.

I just had a little thought when you said that. I just wanted to sort of put out there, too, that there are distributors that put their name on a product, all right, so we call this sort of the own-label distributors. So there are some -- not to further muddy the waters, but there are some situations when the distributor puts their own name on the label; it had somebody else manufacture it for them. So, again, they're putting that product into commercial distribution, and so they're the ones that are then accountable for any complaints, any problems, you know, servicing to the end user. So I wanted to be clear on the point that FDA does have some jurisdiction and reach over distributors, but there are certain circumstances.

DR. ARMSTRONG: Okay. And those are minimal?

MS. WELCH: Well, again, it's sort of -- I think we started the day by saying that, you know, FDA has -- we do have a tremendous amount of jurisdiction over medical devices and over components, but we exercise it judiciously. And we're putting a tremendous amount of the responsibility on the finished device manufacturer. So I just want to be very clear that we do

have more control that we can use, but we don't find that we need to do that.

DR. ARMSTRONG: So when the own label is there from the distributor, does that disassociate the manufacturer from the distributor in terms of ultimate responsibility?

MS. WELCH: It just means, in that scenario, that that distributor then has certain parts of the Quality System regulation that they would have to comply with, number one being the complaint handling requirements.

DR. ARMSTRONG: Okay.

MS. WELCH: It's their name on there, so who is the end user going to go back to? They don't know who manufactured it; they know who distributed it.

DR. ZABRANSKY: I believe that this question more applies to the raw materials and the components that go into a particular product and perhaps items that are outsourced. Is that -- do I have a better -- as opposed to -- which is more or less the end product? Yeah, okay.

So looking at it from that point, so where the manufacturer is responsible for their sources whether it's a component or whether it's raw materials, and one of the things that comes to mind, we talked about earlier, was if these items are coming from a foreign country and then we have the ISO standards that come into effect because of a product coming from Europe

or China or something like that.

Dave, any comments on this?

DR. CRANMER: I think I'm happy that the QSR addresses what it needs to and the specifics of it get dealt with in the various plans that the manufacturer puts together and deal with it.

MS. BLACKWOOD: Liz Blackwood, Industry Rep.

I agree that the QSR covers it. I would say, though, that as industry -- and I'll try to speak for all of industry here, but I know that we go out and we look at our suppliers and we do a risk analysis to determine if we need a second source.

Some of our suppliers sit on a prairie; they have very thin walls and they don't have a big infrastructure, right, but they are important manufacturers, and we can put controls in place. But where they live, you know, in Tornado Alley out there in the Midwest, we have to help them with their business continuity. So we do. Because they're a critical aspect of our business.

So I think it behooves the manufacturer to help the supplier be successful with what we know best, but also to get a second source if it's critical.

DR. KIMBERLIN: And, again, I would say this is addressed throughout the product life cycle, so it starts in design and development about how to identify and qualify the suppliers, how to make sure you've

tiered them according to the risk, where you need a backup supplier, where you need a backup supplier because of geography or the criticality.

And then if anything changes over time, whether like, you know -- so there's usually a quality agreement or some kind of purchasing agreement, then, that goes down to very clear specifications about notification of change or interruption in supply or some kind of disaster recovery.

Because this is -- it's not just a quality issue from a perspective of quality and safety, but it's a huge business cost issue, too. So the business, in order to operate as a business, this is given a lot of attention.

DR. ZABRANSKY: I can think of one specific issue, again speaking of the laboratory, was the source of agar that is used in agar media. It's a specific form of algae that only comes off the New Zealand coast, and it was an El Nino or La Nina that affected it over a couple of years. It was really a problem. And I guess, you know, this affected all manufacturers because they were all getting it from the same area.

DR. CRANMER: Unlike the Department of Defense, I don't think FDA has the ability to compel second source creation.

DR. ZABRANSKY: Uh-huh.

DR. CRANMER: They might like to have that authority and maybe in very critical materials situations --

DR. ZABRANSKY: You mean a backup? Yeah, um-hum.

DR. CRANMER: -- that might be something worth starting to talk to the Congress about having an authority to do that.

MS. WELCH: So this is Jan Welch from FDA.

So one of the guidance documents that I mentioned earlier by the Global Harmonization Task Force on supplier controls talks about that very point, and so FDA was at the table together with industry developing that guidance at GHTF. And we do talk in that guidance document about when the manufacturer sort of needs to audit the supplier's supplier or the supplier's supplier's supplier depending on the criticality of that and of that device.

So yes, the regulation is not specific into what controls there are over suppliers and how they're to be implemented, but we do have this good guidance document that's out there that really does say you might need to consider that.

DR. ZABRANSKY: Ms. Fiore, any comment? Okay.

Ms. Schuenemeyer.

MS. SCHUENEMEYER: As far as purchasing controls, during all of our discussions, the one thing that really caught my eye was the discussion about the nylon 12 manufacturing and it being the only manufacturer for 75% of the nylon 12 that was used, that seemed to me like something that does not apply to Quality System, but it would possibly -- once again, just like Steve said -- be something you may want to consider. The FDA can't say that you

need to have two sources, but -- and where would the other source come from? You know, how would that be created?

The FDA can't say someone go out there and build this. But if Congress were to say that we strongly recommend, as the guidance may say, that you have more than one source for your critical components, then someone would build it, maybe. So it just caught my eye that, in purchasing controls, I think QSR does delineate what needs to be done. But also, it brought to mind wasn't there a problem with -- I don't know if I should say the name -- a drug company with a cough syrup issue several years ago where it wasn't their immediate supplier, it was the supplier of the supplier of the supplier who changed a product, and several people died due to this cough syrup that they -- I think it was a Central American company.

One thing that may be considered is that FDA inspections do involve the suppliers and possibly the suppliers of the suppliers, or at least have a clear route of where did this come from. You don't just say we get this from Company A. Industry might need to, when they engage a supplier, look deeper; find out, okay, we get this from you, where do you get it from, and where do they get it from. And maybe they do that.

DR. ZABRANSKY: I think it's been established that FDA does not have that authority or responsibility, right?

DR. KIMBERLIN: I would add that FDA exercises that authority through the manufacturer and purchasing controls.

So to your point, Terry -- this is Cecilia Kimberlin speaking -- we do, and, again, trace back through the different suppliers to suppliers and sources. And good examples of that was the tsunami where you had this contamination issue in Japan, and you start with the known suppliers and distributors and just started working backwards through that.

And I think that, again, comes out through design, when you do design transfer into the factory, you want to make sure that going forward, everyone knows exactly how those materials are sourced, if they are rare, if it's a sole supplier, and then you put mitigation steps in place to manage that.

MS. SCHUENEMEYER: This sounds again like the QSR is working, as they're written. My only suggestion would be maybe it's something that would be revised in the inspection policies.

DR. ZABRANSKY: Ms. Olivera, any --

MS. OLIVERA: Mary Olivera.

My comment was going to be related to alternate sources, but it was addressed by the Industry Representatives.

DR. ZABRANSKY: Any further comments or questions on this?

(No response.)

DR. ZABRANSKY: Okay, I guess what we're -- some reasons that the QSRs or the regs are satisfactory in that regard, and I don't know whether or not, you know, this can be added, a question of the concern could be added to the inspection process, again, which is not -- I guess, what? Every

several years, depending upon the size of the manufacturer and the product involved.

But is this something that FDA can look into or consider as far as the inspection, that this issue of alternate product source be looked at?

DR. McNAMEE: Are you asking me if the recommendation of the Advisory Committee is acceptable?

DR. ZABRANSKY: Yes, I guess so.

DR. McNAMEE: The recommendation of the Advisory Committee is the recommendation of the Advisory Committee --

DR. ZABRANSKY: Okay.

DR. McNAMEE: -- and we take all recommendations --

DR. ZABRANSKY: Yeah.

DR. McNAMEE: -- seriously.

So if you're recommending the FDA inspect to make sure that purchasing controls are working in order to assure that component manufacturers affected by extreme weather are being duly screened by manufacturers, then thank you for that recommendation.

DR. ZABRANSKY: Well, not only that, but, you know, are alternate sources considered?

DR. McNAMEE: Noted, thank you.

DR. ZABRANSKY: Okay.

So other than that, is FDA -- I guess, any other comments or

feelings about our responses here?

(No response.)

DR. ZABRANSKY: Should we move on, then, to Number 5?

DR. KELLY: How can manufacturers utilize the Corrective and Preventive Action paradigm to effectively re-establish production after experiencing an extreme weather event?

DR. ZABRANSKY: Dave, I'm going to start with you.

DR. CRANMER: Well, I don't know that I have an opinion at the moment. The issues that are involved with reestablishing production after an event like this, I'm not sure that the Corrective and Preventive Action paradigm is the right one. You're almost going back to the beginning and re-verifying that the plant is doing what it needs to do to start with. In that respect, it's more like a re-commissioning of what's going on rather than the way I think about Corrective and Preventive Actions.

DR. KIMBERLIN: Would you like industry to address that?

DR. ZABRANSKY: No, let's move -- Dr. Armstrong, any --

DR. ARMSTRONG: Brenda Armstrong.

This is 820.1, right, in the regs? It really would be starting from scratch. And I'd have to ask if that's an appropriate way, if a manufacturing plant is completely blown away, do they go back to square one and start all over again?

MS. BLACKWOOD: Liz Blackwood, Industry Rep.

Okay --

DR. ARMSTRONG: So if that was the case, it would seem that it is an appropriate -- it would be an appropriate model or paradigm if that's the case in an extreme event.

MS. BLACKWOOD: It's kind of all we've got, so we would use it, I would say --

DR. ARMSTRONG: Okay.

MS. BLACKWOOD: -- if I could speak for industry, and that is -- and it may end up being preventive in nature, which we do more corrective than we do preventive, just on the whole, but -- so you would do an investigation, which is part of CAPA, and you might determine that everything's running per parameter; you do some kind of inspection to make sure there's no damage of any kind. And then from a preventive standpoint, you've done that inspection and determined that it's still suitable for use. You might inspect, investigate, and find out that it's not; and we would use the CAPA system to do that.

DR. ZABRANSKY: Okay. So a plant was virtually destroyed during a disaster of some sort, and now they've rebuilt the plant and they're going to reopen and remanufacture. Is this now subject to a brand new inspection by the FDA or --

DR. KIMBERLIN: Could be, yeah. Again, this is Cecilia Kimberlin, Industry Representative.

So, you know, events vary by order of magnitude and severity. A plant being eradicated upon an event like that is a major event which would certainly enter the Quality System into the event being documented and management appropriately meeting, identifying all the containment issues through non-conforming material and potential issues, and then you get to the point where what was the root cause, a tornado or hurricane or whatever it was, and what are we going to do about it.

And the Corrective and Preventive Action system would be very effective there in managing this kind of global -- you know, driving management to do all of the actions it needed to reinstate and be able to once again manufacture according to the device master record. So if it necessitated repair of the plant, revalidation of equipment, reordering equipment, so you go through all those stages again. It would be massive, but it has been done and would be done.

If the scale of the event was less, then less action would occur. And then before you went back into production, you would have to have, again, all the verification steps that both the materials and the processes met their specifications. So this is not something that would occur very rapidly, but those are the steps that you would go through. And I think the current regulations address this both from CAPA as well as other parts of the QSR.

DR. ZABRANSKY: FDA, has there been any inspections concerning companies or factories that have been destroyed from Katrina or

most recently, the New Jersey/New York situation? Are you aware of any inspections that had to be done or were done? You know, putting a factory back on line or a production plant back on line?

DR. McNAMEE: Scott McNamee, FDA.

Not specifically. I know that there were a number of device firms in the area that were impacted, but as we learned from Captain Lewandowski-Walker's presentation, there's a certain triage with regards to inspectional resources. Ordinarily, the district office will contact the device firms by phone and inquiry them, you know, "Big storm, how did you do, everybody okay," that kind of reaching out. At least, that's my understanding of what usually happens within the districts.

DR. ZABRANSKY: Ms. Fiore, any -- no. Thank you.

Ms. Schuenemeyer. No?

MS. OLIVERA: Mary Olivera.

I think the CAPA section is pretty detailed, and if combined with the process validation, I think this is well written.

DR. ZABRANSKY: Well, I guess in summary, the Committee, I guess, feels that the current regulations and what the manufacturers are doing meets their needs, as well as what perhaps is addressed by FDA. I don't see here any concerns.

Does FDA have any further comments or -- no.

I guess we can move on to Number 6.

DR. KELLY: What additional steps or successful practices might firms take to maintain and monitor the quality of products or mitigate damage to products from extreme weather events during storage or shipping?

DR. ZABRANSKY: Let's start over here on the right this time, and we'll go to Ms. Schuenemeyer.

MS. SCHUENEMEYER: I think that we discussed this question when we were talking about -- was it Question 4, when we were talking about distributors and --

DR. ZABRANSKY: Um-hum.

MS. SCHUENEMEYER: -- I think we covered pretty much what the group feels, that the QSR is satisfactory and additional steps or practices that firms might want to maintain could be handled potentially with design controls or design changes in products to provide some sort of warning system that this product went through a bad event, don't use it.

DR. ZABRANSKY: Ms. Fiore. Push your button.

MS. FIORE: My impression is that industry has this well covered and FDA has this well covered under the existing regulations and so on.

DR. ZABRANSKY: Industry, Ms. Blackwood.

MS. BLACKWOOD: Liz Blackwood, Industry Rep.

I wrote down a couple things earlier as I was going through

because you could say the regulation covers it, and I think it has allowances for that, but we do have, especially in the bigger corporations, business continuity programs. And business continuity programs are assessments that every factory has to go to on a periodic basis to determine if their preservation of records, IT infrastructure, "do we have generators," tested, you know, go through a drill, right. Shut everything down, see if things come up, "do we have enough gas in the tank," right.

So we have drills and continuity and backups and certain redundancy measures depending on how catastrophic would it be to the business if we had to either lose information and need to recreate it, lose product, need to recreate it. And so I think it's broader than just about the product; it's about the whole business.

But business continuity programs are not something new to the industry, and I think that would be what I would call successful practice that I would share beyond the regulation; that I think, you know, it depends how much you can afford.

Now, small business maybe doesn't have this, but they can't afford it and they're taking their chances they may lose their business, right? So that's what we call business continuity programs, and then supply chain risk management is like an element of that where you assess "do I need a backup supplier, do I need a second source or a second location," and that type thing.

DR. ZABRANSKY: Dr. Kimberlin.

DR. KIMBERLIN: Cecilia Kimberlin, Industry Rep.

I would just add to what Liz is saying, that, you know, whether you call it continuity or disaster recovery, we are required to have this by others who come in and look at our enterprise systems and other -- for other reasons.

And just one thought I might suggest for consideration by the Agency -- Jan and others talked about existing guidance for manufacturers applying the GMP -- would it be advantageous to have some guidance, even if it's a sentence or two, about -- under management responsibility and management controls, that there is consideration given in either the quality planning process or other subparts of the regulation to specifically address disaster recovery and how that would affect product and processes, and then just leave it at that?

And so, you know, we put quality systems in place, we do quality planning, we do auditing, we do all the other things, training and resource allocation, under management controls across the entire Quality System, and would bring some attention to it. I agree with Liz. I think it's done, but I'm just wondering if there would be some consideration that we could get a better level of playing field over time if it were introduced as one of those incremental pieces to existing guidance that we talked about earlier.

DR. ZABRANSKY: Again, the last two words on this question

relate to storage and shipping, which is, I guess, we discussed before. So that brings up the issue again of packaging, again. But that, in turn, goes back to design control.

Ms. Olivera.

MS. OLIVERA: Mary Olivera.

I think we've discussed packaging over and over, and it all boils down to for controls and transporting and visual signs that the package has been compromised.

DR. ZABRANSKY: Dr. Armstrong.

DR. ARMSTRONG: I don't think I have anything else to add.

DR. ZABRANSKY: Dave.

DR. CRANMER: This is a place where a forward looking at different technologies to be those visual indicators that something has happened may be worth a study or document from FDA about what you see that might be possible.

DR. ZABRANSKY: I guess what I'm hearing is that there are two aspects here, is this issue of management and whether or not that has to be added to the regs. I hate to see you have to go through, just to add one or -- you know, one more paragraph on that or whether that can be adequately handled in guidance documents.

DR. KIMBERLIN: Just a comment. I wasn't suggesting the regs would require it because I think the regs outline management control very

well, actually.

DR. ZABRANSKY: Um-hum, yeah.

DR. KIMBERLIN: What I'm suggesting is that to include the Quality System as part of the business' overall continuity or disaster management plan and that it be reflected in the Quality System according to the subparts we've identified.

DR. ZABRANSKY: Um-hum.

DR. KIMBERLIN: Thank you. Thank you for the opportunity to clarify.

DR. ZABRANSKY: Yeah, okay.

Any further comments?

(No response.)

DR. ZABRANSKY: I guess the concerns have been addressed to that.

FDA, any -- okay.

We move on, then. Number 7. This is kind of a related question to what we just had here.

DR. KELLY: What should firms consider with respect to their Quality System after an extreme weather event in order to be proactive for future events?

DR. ZABRANSKY: All right, we're going to start now with industry this time.

DR. KIMBERLIN: This is Cecilia Kimberlin, Industry Representative.

I might just describe what I think is a best practice, and just as we do post-product design reviews after launch and over periods of time to see how well did we do and what we've learned and what we got right and what we could get better, when we -- you know, I have experienced the practice of after such an event that is certainly quite big and catastrophic and requires a lot of resources, once we are far down the road and we think we've accomplished our goals, we sit down and evaluate: Did we do all right? What could have gone better? What changes do we make in our own system that would make this work better?

So, again, I don't know where something like that fits, but I think that kind of evaluation is a very good management practice.

DR. ZABRANSKY: Ms. Blackwood.

MS. BLACKWOOD: I would agree with Cecilia in that maybe bringing that to the quality management review, which is a required periodic review. Some locations we do it depending on the level, monthly, sometimes we do it quarterly, and sometimes we do it ad hoc, and I mean, to actually call it a quality management review and come in and sit with the senior managers to debrief on how things went, I think that would be a good way to utilize the QSR.

DR. ZABRANSKY: Is this sort of thing addressed in operating

procedures for companies? Okay. Because these are normally looked at.

MS. BLACKWOOD: Yeah, our sole -- yes. We try to share practices so if something happened in one business, when we come together across multiple businesses, we have a time for sharing common themes or for sharing unique themes that we should be, you know, proactive in other areas about.

So that's why I selected the quality management review because I think that is a time when you do get senior management and you do have an opportunity to share ways and means to prevent. That's really the purpose of the review, is to check the health and welfare of the quality management system and then to assure that you're proactive.

DR. ZABRANSKY: Ms. Fiore.

MS. FIORE: Well, I agree with what has been said by industry, but I also think that a look-back should be done on an individual basis of every incident.

DR. ZABRANSKY: Ms. Schuenemeyer.

MS. SCHUENEMEYER: I agree with what industry has said. It brought to mind, though, the emergency management systems. Paramedics, hospitals, emergency rooms have drills to prepare for disasters, and what popped into my head, when I was listening to what was just said, is after something happens, they meet and discuss what happened and how could they prevent it moving forward.

I guess, as the Public Representative, my initial reaction is I'd like to see a more proactive response and rather than wait until after something has happened, perhaps part of their -- not necessarily the regs, not a change in the QSR, but perhaps a change in the management control. They plan for these things in advance and have drills.

What would we do to prevent things from being damaged? Would we stop shipment? If a hurricane is coming to an area, would we stop shipment early so that possibly those products aren't damaged? And I would leave that to industry to work out what the drill should be, but I think I would like to hear that something more proactive was put into place.

MS. OLIVERA: Mary Olivera.

I guess my question to you would be is this review or lessons learned a corrective plan that you put in place, is that based on, like, in a standardized criteria that you always look at and is the same for everybody, or you choose and pick what things are going to be reviewed?

DR. KIMBERLIN: We do have procedures and we do delineate within the company what we look at to make sure that the overall management of the Quality System is effective, which means we have safe product. We actually provide product on a reliable basis. So, yeah, it is prescribed and -- but not to a point, you know. I think to go back to Liz Blackwood's comment, you know, we also have portions of the management review which allow new issues to be brought forward like new

regulatory changes, new events.

The procedures that are in place are intended to be proactive to meet these events, but the objective of the Quality System is to continuously improve and prevent these things, so we would bring those types of actions up at the management review. We would agree on action items, and then those action items would be tracked and implemented according to procedure.

DR. ARMSTRONG: I just have a question. In 820.22, the Quality audit, is that what that is? Okay, that's not. So --

MS. BLACKWOOD: In that same section.

DR. ARMSTRONG: Yeah.

DR. KIMBERLIN: In the same section, Management Review.

DR. ARMSTRONG: Okay, all right.

DR. CRANMER: I don't know that I have anything really to add at this point. I mean, this is all the stuff I'd put in a category that, for most manufacturers, I'd call continuous improvement, and it applies not just to Quality System, but to everything you do. And I don't see that this is any different in that respect.

DR. ZABRANSKY: I guess, to kind of sum up what we've discussed in regard to this particular question, I guess the issue of management has come up again, you know, how can FDA further emphasize or encourage industry to review their management practices, their SOPs, and

so forth in this regard. Companies do it.

Is this something -- you know, I don't know whether it should be put in -- originally, we were discussing guidance documents, but a lot of that had to do with design and so forth of the products. What we're talking about here is the overall operation of the manufacturer. And being proactive, I guess, so often I know that, working in a hospital, you're crisis oriented. This is not where we want to be. We want to be proactive on everything that we're doing.

Any other concerns that FDA has? No.

Okay. Number 8.

DR. KELLY: Are there elements of the firm's Quality System that FDA should highlight in inspections of manufacturers following an extreme weather event?

DR. ZABRANSKY: All right, now I guess we'll look at the specific elements in the inspection process. We haven't really discussed inspections that much. And, again, I don't know -- only, again, industry is going to be aware of what constitutes the inspection, but the user doesn't know, as a rule, what the FDA is inspecting.

So I'm going to start over here. Are you aware of anything that goes on, Dr. Armstrong, with inspections?

DR. ARMSTRONG: No, but I do want to make a comment about this in particular. If there is an extreme weather event, it would seem that a

debrief that might actually uncover something that wasn't known or wasn't suspected ought to somehow get back or be part of a plan to address it and to communicate that to the FDA, especially since -- again, it starts and stops with you all in terms of that purview, but in terms of the general good to the population, if there was something that was found out that could be, one, corrected, then that ought to be published in some way in order to provide guidance for a future event that is of similar magnitude.

I guess I said that right.

DR. CRANMER: I don't think there's anything that I would say needs to be highlighted. I think the issue becomes more the inspection resources available to FDA to do it in the first place, and that sort of falls outside the purview of this committee because we can recommend, I suspect, that more resources ought to be devoted to it, but I can't make the Congress appropriate money to do it.

DR. ZABRANSKY: Well, the question that I would ask at this point is during an inspection process following a disaster, is information provided by the FDA to the consumer about a particular product or problem with a manufacturer, or is it just through the recall process?

MS. WELCH: Well, I think I want to just clarify the question a little bit. What we were trying to ask here is you've heard a lot today, for those of you that may not be as familiar with the Quality System regulation, you might know a little bit more about it than you did, and others are well-

versed in it.

But I think what we're trying to ask here is, of the requirements, the things that we've highlighted that you've heard today, is there something that you believe should have more emphasis in an inspection? I'm not talking about numbers of inspections or the whens and the hows, but with respect to the elements of the Quality System that we should pay particular attention to, in your opinion.

DR. KIMBERLIN: This is Cecilia Kimberlin, Industry Representative.

If we step back and think about the earlier presentation on the types of inspections that are done, this would probably be one of those special types of inspections. Even if it's based on the QSIT, the first thing that's looked at is the Corrective and Preventive Action system. And in that discussion, the investigations looked at were you global enough, so I really believe that, based on the Agency's approach, whether it's for a cause like a special event that this may -- would this fall under, I guess, a special event, this type of inspection, if you came in after a big disaster like this? Does the Agency have --

MS. WELCH: This is Jan Welch.

Clearly, if you read the compliance program, you're not going to see an extreme weather event, so "for cause" is not really captured in that regard. It's not our traditional thinking, but we can take that under

consideration.

DR. KIMBERLIN: No, I mean, I'm just wondering, you know -- then you would consider this a routine inspection?

MS. WELCH: This is Jan Welch from FDA.

Yeah, I think it's going to depend on are we going in to -- why are we going in?

DR. KIMBERLIN: Right.

MS. WELCH: We don't go in just to go in. You know what you're doing and what you need to do. Is it something sort of a site change, you know, you've rebuilt?

DR. KIMBERLIN: Yeah.

MS. WELCH: Yeah, you've relocated, you've changed facilities, so in the context, would it trigger, you know, the site change and it would trigger an inspection. But, you know, we're not going to go out as a matter -- in an event like this just to do an inspection at every place. We're going to rely on why is the need, why would we need to be going out there. If you need the time to let your QMS be --

DR. KIMBERLIN: Right.

MS. WELCH: -- functioning and working --

DR. KIMBERLIN: I would agree. That was my thinking, as well.

MS. WELCH: Okay, all right.

DR. KIMBERLIN: I just didn't want to say this and have --

MS. WELCH: Okay.

DR. KIMBERLIN: -- the Agency thinking differently about it.

The other thing I think is important to point out here is that in such an event, we would already be in communication with our district offices, not only at the location of the geographic area where the event occurred, but probably other district offices where we might be wanting to get product from those sources, if we have multiple plants making the product or for other reasons, for distribution or whatever.

So there would be ongoing communications with the Agency, and I like the idea of the industry being able to come forward and present their plan to the Agency in a proactive, full way so that the Agency can have the assurance that the firm is addressing this. And then, like Jan said, maybe later, in case they have to do a product approval or whatever, they could come in on inspection.

So it would be really good to have full communications around such an event, after it occurs, with the Agency, and a planning process so that both sides can be assured that we have time to implement correctively. You see our plans, and then if you need to, you could come in and inspect at an appropriate time.

DR. ZABRANSKY: Ms. Fiore. No comment.

Ms. Schuenemeyer.

MS. SCHUENEMEYER: I think that if we were to have to pick

some of the Production Process Control, Environmental Control, Purchasing Control, I think that if there was an inspection following an event like this, that the Corrective and Preventive Action would be an important focus, probably the most important focus. What did this industry do to get back on line? And I think that would probably answer the questions about the other areas.

DR. ZABRANSKY: Ms. Olivera.

MS. OLIVERA: Mary Olivera.

I would focus on that corrective, the CAPA, and the process validation because after a major weather event, you want to make sure that everything is back to where it should be. And I want to make sure that the product that is produced is at the same quality that it was before that event happened.

DR. ZABRANSKY: Any further comments?

(No response.)

DR. ZABRANSKY: I guess in summary on this thing, what we heard at the very end here has to do with the CAPA approach to this thing, to correct. What did the company do to correct it? Did they do a proper examination of any failures if they did occur, any that led up to the problem?

At the same time, the other thing I brought up a lot earlier had to do with record keeping, you know, where are the records being kept, are they still viable and searchable, or are they in a closet someplace, maybe

where they're safe, as long as they're not being lost.

Any other concerns from the Committee?

(No response.)

DR. ZABRANSKY: FDA, do you have any comments concerning these comments? No.

Number 9.

DR. KELLY: What is the appropriate balance of manufacturers' resources and staff time in anticipating and preparing for risks of Extreme Weather events?

DR. ZABRANSKY: This is an interesting question. Let's start with NIST.

DR. CRANMER: This is one where the answer really is "it depends." If you're a bigger firm, you have more resources and staff to throw at all the issues that might come up, but it's probably already treated pretty much as part of your risk mitigation in the first place. So you've already hit that balance.

As you get to smaller firms, the chances of your applying an appropriate balance is probably pretty small to start with because people working in that smaller business are busy working in the business to get stuff out the door and not spending as much time as they should on the business in trying to see the future and prepare for it. So that's where the "how might we help them get a better balance" without specifying exactly what that

balance is because it depends on the business.

DR. ZABRANSKY: I have a question for the FDA in relation to inspections of a smaller company. Are they handled any differently than with a large company, where you may have an individual wearing multiple hats in a small company?

MS. WELCH: This is Jan Welch from FDA.

No, we conduct our inspections, whether it's one of these Level 1, 2, or 3 QC inspections the same way every time.

DR. ZABRANSKY: Dr. Armstrong.

DR. ARMSTRONG: I agree. You know, a lot of this is determining the magnitude of the event or the forewarning that you have for the event and then deploying resources in line with what the event is projected to be. So to me, it was whatever time and effort it takes, knowing the magnitude of what it is you're up against. It's no different, I would assume, from the manufacturer than it is for the target of the actual event.

We did that with Hurricane Floyd in the hospital. We knew it was coming, we knew what we had to expect, we knew what resources had to be deployed ahead of time, and I would think, on the other side, anybody who is providing us with supplies or with expertise would have that same level of concern and intervention, so it really would depend on the perception of the magnitude of the event and in the forewarning and planning to deploy appropriate resources.

DR. ZABRANSKY: Dr. Kimberlin.

DR. KIMBERLIN: I would agree with that. I think, you know, again, with the idea of having these reviews in place and a management team that's been identified for crisis management, when these potential issues or real issues are coming forward and we have some early information about this, you know, hurricanes in Puerto Rico that might affect our factories, then action goes into place.

But it's, again, based on the event, and it's really hard for me, when I looked at this question, to answer what's the appropriate balance. And maybe if there's some clarity around what are we seeking with this question, we could address it further.

DR. ZABRANSKY: Ms. Blackwood.

MS. BLACKWOOD: Liz Blackwood, Industry Rep.

I think it's a little bit of a different approach, depending if you're anticipating this during design, early, before even there's a weather event on the grid or if we know that there's a weather event coming. I think when you go design-wise, we really do need to stratify the risk of the devices that we think we want to do a little bit more for, we talked about that earlier.

I do think, when it comes to there's something on the weather grid, it's "everybody's in." That's just how it works, right? Hospital, manufacturer, office. It's everybody does what they need to do, and you shut things down and you make urgent plans depending on the nature of what's

coming and what could be the impact.

DR. ZABRANSKY: Yes, fortunately in the case of weather, you get some advance notice. But, again, in the case of an earthquake or, we mentioned earlier, a nuclear accident in a nuclear plant nearby or something of that nature, you don't get that much warning.

Ms. Fiore.

MS. FIORE: Edna Fiore.

This is something I think should be coordinated with FEMA.

DR. ZABRANSKY: Ms. Schuenemeyer.

MS. SCHUENEMEYER: Terry Schuenemeyer, with the Public Rep.

I think the key word in this question is "anticipating," and I think that hospitals, manufacturers, FEMA, everybody needs to accept the mindset that there have been more and more of these type of disasters, and I don't think it's just that they're being reported more, although having a tsunami live on television does catch your attention, whereas 50 years ago, hearing about it two days later, it may not have brought that much attention to it.

But I think that manufacturers, whether small or large, should -- I would like to see that they are required to, in some way, anticipate that something could at some time happen depending on their geographical locale. If you're on the Gulf Coast or in Florida, South Carolina, you should

anticipate that you, at some time, will have a hurricane. If you are in the Tornado Alley, then you might want to anticipate that sometime you may be hit by a tornado. If you're in California, then your process may be disrupted by an earthquake.

So I think that they should anticipate that something could happen, and whether they're a large company or a small company, I don't know that that matters. Small companies may have an advantage. If you have 10 to 20 employees, you can get them into one room and discuss this all together and say, look, what if we have an earthquake? What are we going to do? What processes -- do we need to have drills, do we need to -- you know, how will we review our processes, how will we get back on line, whereas mega-companies, that could involve, you know, 100 people in different locations and multiple meetings and a lot more of their time and resources, which -- but it sounds like they have processes in place.

But it just kind of, once again, brings back the idea that perhaps the regs are fine, but the management control needs to have even one statement that says management must consider that you at some time, as a manufacturer, may experience an extreme weather event and you must plan for and prepare for it. May be vague, just like the regs are, and let the industry do their own work, but I think that it's something that -- it's not going to go away, and it's not going to lessen. I think that predictions are that we're going to have more and more of these extreme weather events.

DR. ZABRANSKY: Ms. Olivera.

MS. OLIVERA: Mary Olivera.

I think the emergency preparedness plan of every manufacturer should address these major weather events, and the associated effects of each and every one of them based on their location, as well as their staffing responsibilities in those events and/or in some cases, there are companies that outsource some of their cleaning or resources when an event happens, let's say a flood. I know the company will come in and help them clean out. So I think all of that should be part of an emergency preparedness, they drill or practice every so often just like we do in a hospital. We prepare for every instance and practice.

DR. ZABRANSKY: I guess what I'm hearing is although there may not be problems with the regs, that nevertheless there should be some recommendations either through guidance documents -- I don't know if that's the appropriate place to put -- encourage companies to be more proactive in their planning for emergencies of one sort or another.

Again, you can't use specific terms like a weather event, which may not affect one part of the country but, you know, just the general term of weather or disaster. It's going to obviously depend upon the nature or the extent of the event as well as the size of the company, where it's located.

Any further comments? No.

FDA?

(No response.)

DR. ZABRANSKY: Do we have any more questions?

DR. KELLY: Last question: Are there other recommendations for the FDA in light of extreme weather events?

DR. ZABRANSKY: Do we want to see any further changes to the regs or any other further guidance documents or modifications to any other documents perhaps that have not been mentioned? How many were there, did you say?

MS. WELCH: This is Jan Welch from FDA.

As I said, some are reference materials we prepared, so we'd have to go back and look. But I know at the time that we drafted the regulation and put it out there, we prepared probably 10 to 12 different types of documents for small manufacturers and for others, and many focused on design controls because that was the brand new feature of the regulation, where a lot of this risk work is. So I don't have a specific number, but I'm going to say I could probably go back and pick up about 10 or 12 FDA, and a couple of the GHTF, guidance documents that are pertinent.

DR. ZABRANSKY: Ms. Olivera, do you have any --

MS. OLIVERA: Perhaps new technology. We keep on evolving so quickly, and today we're here and write a document, and a year from now it is already obsolete or needs revision because technology evolves so quickly. So somehow incorporate the new technology and inspections and the quality

process and so on.

DR. ZABRANSKY: Ms. Schuenemeyer.

MS. SCHUENEMEYER: I think, from what I've heard so far today and yesterday is the FDA -- my recommendation to the FDA would be risk-based, as we discussed; critical products, whether they are home based or whether they are Class III devices; come up with a risk strategy; and sole manufacturers, suppliers.

These seem to be recurring issues that are of concern, of more concern than whether or not manufacturers have their processes in place and are based on the QSR. I think the QSR is fine the way it's written. I think that manufacturers should be made aware that these events are out there and they're going to keep happening; they're going to affect you, they're going to affect your supplier, they're going to affect your devices as they're being transported.

And I think that guidances may be the way to go as long as there is at least a strong recommendation that all manufacturers have something in place in the management level, that they look at this as a potential that is going to happen to you at some time and that there is a plan that is ready and that it's practiced for.

And then I think that as far as inspections go, the CAPA area probably is where the resources could be put after these events: What did you do to correct the problems that you saw, whether it was revalidation of

an entire facility or retesting of a contaminated water source. And I think that the regs, as they are, probably should stand.

DR. ZABRANSKY: Thank you.

Ms. Fiore.

MS. FIORE: Edna Fiore.

Well, I concur with everything that was just stated, but I also think that emphasis should be placed on the cutting edge technologies.

DR. ZABRANSKY: Thank you.

Ms. Blackwood.

MS. BLACKWOOD: Liz Blackwood, Industry Rep.

You know, I was thinking back to Dr. Kelly's facts that she shared with us and when you think of over 100 events in 30 years -- and I suspect if you measured the mean time between events and the magnitude, it probably gets more severe over time, because things are getting weird, right, with the weather. We've seen some just weird things in weird places over the last 10.

But being of the size that Abbott is and that Johnson & Johnson are, if there are three events happening every year, chances are we're experiencing at least one. So we know why we have disaster recovery, and we know why we have risk analysis of our supply chain and why we determine whether or not we need second sources because we face that every year, we do.

So if you have one site or five sites or something, you may never experience this, and it may never impact you, but I do think that there's an aspect of, besides the regulations, which I think force us to investigate and fix and revalidate and review and reflect and fix and so forth. We could share, as an industry.

That's one of the recommendations I would have you put before -- you guys -- before we put something out in the industry as guidance, get together and talk about the possibilities and what would the impact be and how could smaller manufacturers learn from larger manufacturers and what's the right thing to do and maybe have some kind of a sharing venue. I mean, it doesn't have to be in person; it could be a WebEx or different ways and means to do that.

But, you know, you can't imagine investing in something that you've never experienced before, so it could be sharing the facts and data, and then sometimes it's just about, hey, you want to take a chance of losing your records or your business or your product, you weigh out the risks, as a business. We can't do that.

DR. KIMBERLIN: Well, I agree. This is Cecilia Kimberlin, the other Industry Rep, and I agree with what Liz has said.

I think the other recommendation that I would put forward to consideration, which ties to the Quality System, but beyond that, and that is that when these events occur, the first interaction between the Agency and

the firms, whether it's an anticipated event or after the fact, is with your local offices. And so is there anything that we haven't thought about there that we could recommend?

You know, let's say we become aware of something, let's take it out of the weather frame, but it's a significant event. What can we do to have industry and the Agency work more transparently together, more effectively together? I don't have any point to say, well, we haven't worked effectively together, but I'm just thinking, again, in anticipation, if that's where the communication and the touch points start, maybe feeling more assured that the Quality System regulations are pretty thorough, do we focus some attention there?

And I think that would help both industry and the Agency enhance these communications, and then we would get to the point that Liz said where we'd have more sharing of information. I mean, the Agency frequently presents at industry meetings, open meetings, on best practices and recalls that they've seen and other things that they share, and this would be a great forum for industry and FDA to get together and share this information.

MS. SCHUENEMEYER: I agree with that completely. I'd just like to add that, from the standpoint of someone who works in a major medical center, when Katrina hit New Orleans, the population of Houston increased in two weeks by almost a million people. And those people, a lot of them were

patients that all of a sudden had been relocated and needed to be cared for by physicians who didn't know their medical history and could not acquire their medical history from their providers because the providers were gone, the facilities were gone.

The devices -- I'll keep it to devices, not drugs -- that they may have had implanted in them, we may or may not have had the necessary equipment to test them or care for them. The durable medical equipment may have been in place, but the volumes were overwhelming. And this is probably handled under GCP, but the clinical research patients were -- all of a sudden, had no one that was on their study, had no one who knew about their product or could handle their product. And I think that any future conversations should also consider the hospital side, the person who is taking care of these patients whenever these events happen.

DR. ZABRANSKY: Dr. Armstrong.

DR. ARMSTRONG: I don't think there is any way to be too proactive where catastrophic events occur. And to identify and disseminate best practices and to do it immediately and come back and make sure that there is surveillance, that whatever was a learned lesson was, at very least, considered for implementation on both sides so that the manufacturers take away that information and that there's a lot of crosstalk.

One of the things that is the most frustrating when you are the person dealing with a product, a device, where you get the device and then

you feel like you're abandoned. It doesn't happen all the time, and the best and larger firms actually don't usually abandon you because there's someone you can identify to harass.

(Laughter.)

DR. ARMSTRONG: But for small firms, they many times disappear, and so that crosstalk has to occur often at a predictable time where there's the ability to exchange the best practice, identify what it is, exchange it with both the manufacturer as well as the group of people who are receiving that information. And that ought to happen, given how rapidly things are changing in biomedical science, that ought to happen anyway in a time period that's no longer than 6 to 12 months.

And I don't know whether that is something that is part of guidance. Certainly, I would not prescribe it in a reg, but certainly, on both sides, there ought to be very frequent crosstalk and modeling in conjunction with engineers or scientists who can tell us the worst case scenario, allow us to think outside of the box in terms of "what ifs" to support what's left over after the event occurs. I don't think we have seen anything near what's coming in the future.

I just don't think any of us, as forward-thinking as we think we are, none of us imagined Sandy and none of us have imagined anything until they happen, and so we are always reacting. Well, we have the technology and the brain power here amongst scientists in terms of modeling that we

ought to be much more proactive and then design an adaptation for both that allows us to minimize the destructive aftermath just because we weren't smart enough to think about it on the front end.

DR. ZABRANSKY: Dr. Cranmer.

DR. CRANMER: Dave Cranmer.

There are about three things left on my list.

One, the QSR, by itself, is fine, but as we think about revising guidance documents, it's not just the extreme weather events you might consider advising against. It's any disruption of operations like the airplane that falls out of the sky or the toxic chemical spill that might force an evacuation and any of those potential risk factors need to be included.

Another one, and this one for the FDA, is maybe the creation of a training or simulation course or module or a video based on the experiences of those who have been through extreme weather events that you can share with those who haven't or maybe are in less likely areas to do it but someday it could happen.

And the last one has to do with the protocols for the smart durable medical equipment or anything else you're going to put sensors and communication devices in. As I was listening to that, I can think of lots of benefits to the manufacturers to have that information and lots of benefits to me, as a potential patient, to have those, which I hope I never have to do, but it wouldn't be surprising to me if I did.

But the protocols about when that communication is activated and by whom reminded me that there are people who don't want to be tracked, so that just needs to be part of the communications protocol as to how that gets dealt with and who owns the device, who owns the information that comes from it and it's treated appropriately.

DR. ZABRANSKY: Thank you.

The only thing new I heard in what -- I guess, particularly what Dr. Cranmer mentioned, it was this business about training and so forth, and I think again of emergency planning, they do have tabletop exercises where they go through these sorts of things. And I don't know whether or not that's, again, within the purview or the responsibility of the FDA. Definitely, it's part of FEMA -- and whether or not FEMA can be encouraged to work more with manufacturers and so forth, including them in these types of exercises.

To sum up, I guess -- we've had no changes, I guess, we're recommending on the regs, as a rule, but guidance documents were addressed a number of times of where some of these things can be -- and I don't know if I have them all here, but we talked about perhaps addressing sensors and so forth on DMEs.

We talked about encouraging industry to consider universal-type batteries or universal power supplies.

Talked about being very proactive in everything that we're

doing in regard to emergency preparedness, taking into consideration risk stratification for the device, as well as the risk associated with an extreme weather event, no matter what it is.

We heard about sharing between companies of their best practices and approaches to things.

We heard about, definitely about, management applications to handling the events, as well as -- what do I have down here? Being proactive in CAPA and so forth.

And then the issue I brought up a couple times of record keeping, of how that's being handled.

I may have missed over some things or glossed over some things. If any of the Committee wants to add some other comments?

(No response.)

DR. ZABRANSKY: Okay. At this time, we would like to hear some comments or summations from the FDA, if they have any.

DR. McNAMEE: Thank you, Dr. Zabransky.

This is Scott McNamee.

I would repeat what you just said, but you said it so well and it's in the transcript; I don't think I need to.

I would like to take this opportunity, though, to thank everyone who participated today. I know it's a sacrifice of time, and oftentimes traveling is difficult, and please know that all of your efforts are very much

appreciated.

This is the Devices Good Manufacturing Advisory Committee, but I can tell you that the work that we're doing is being looked at, as you can see, from an Agency perspective, from a department level, as well. And the work that Dr. Kelly has done to reach out to our colleagues across the government that also have work in this type of area has been excellent, and we're good at sharing and we like it.

And we appreciate that there may be things that come up on your way home that you think "Oh, I should have said such-and-such. Oh, we need to highlight this aspect." There is a docket that is open for public comment, which is a much broader docket in the area of extreme weather. It's up on the screen there, and it's also in your materials that were handed out. So if afterwards you or any of your colleagues would like to contribute to that docket, we do encourage it. All of it is going to be taken into consideration, and I know that there will be a summary posted tomorrow of this meeting.

In the future, look for other opportunities to interact with the Agency in this area because I know today is not the end of it. There is still a lot of work to be done.

And, again, thank you for all of your help.

DR. ZABRANSKY: Well, lastly, I would to thank the Committee, everybody that's been here and their contributions. It's been a pleasure to

meet with you. We enjoyed your contributions.

I didn't see here, too, any rancor, which is excellent. If you've ever been to some of the other device meetings, there has been sometimes some rancor about some products.

So at this point, I'd like to say the meeting is officially adjourned. Thank you.

(Whereupon, at 4:38 p.m., the meeting was adjourned.)

C E R T I F I C A T E

This is to certify that the attached proceedings in the matter of:

DEVICE GOOD MANUFACTURING PRACTICE ADVISORY COMMITTEE

April 11, 2013

Gaithersburg, Maryland

were held as herein appears, and that this is the original transcription thereof for the files of the Food and Drug Administration, Center for Devices and Radiological Health, Medical Devices Advisory Committee.

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CATHY BELKA

Official Reporter